

Recontextualising the lived experience of hepatitis C and its treatment

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Recontextualising the lived experience of hepatitis C and its treatment

David James Whiteley | December 2016

A thesis submitted in partial fulfilment of the requirements of
Edinburgh Napier University, for the award of Doctor of Philosophy

Abstract

BACKGROUND: Rapid advances in the treatment of the hepatitis C virus (HCV) have been witnessed in clinical practice over the last five years. Pharmacological developments have ended the reliance on the drug interferon- α as a component of successful therapy, heralding the dawn of a new era in the fight against the disease. How this new era is being understood and experienced by those individuals living with the virus is currently unknown.

METHODS: A purposive sample of 20 individuals participated in face-to-face semi-structured interviews exploring their experience of living with HCV. Eight of these participants were interviewed again following a period of interferon-free treatment. All interviews were conducted between June 2015 and March 2016. The interviews were transcribed verbatim and explored using thematic analysis, underpinned by social phenomenological theory.

RESULTS: Analysis of the corpus of data resulted in three overarching themes entitled 'positioning HCV', 'beyond a physical burden' and 'reconstructing uncertainty'. These themes offer original insight into how this new era of therapy is being realised by those living with the virus. The experience of interferon-free treatment was also explored through the narratives of those individuals who participated in a further post-treatment interview. Three further themes entitled 'expectations and realisations', 'an honour and a pleasure' and 'treatment needs' encapsulate their experience.

DISCUSSION: The findings from this study recontextualise the lived experience of HCV within a new era of treatment. In doing so, they expose social and emotional spheres of illness, and a perception of illness chronicity, which remain untouched by the treatment revolution. Further, this work emphasises how treatment inequalities fundamentally underpin multiple aspects of the daily lived experience, and are integral to how those living with HCV articulate the disease. The implications of this work challenge current HCV policy and clinical practice.

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Finally, I am immensely grateful to the participants of this study. Their candour, openness and generosity of spirit made this thesis what it is.

Table of Contents

| | |
|---|-----------|
| Chapter 1: Why hepatitis C, and why now? | 1 |
| 1.1 Introduction | 1 |
| 1.1.1 Thesis aim and rationale | 1 |
| 1.1.2 Thesis structure | 1 |
| 1.1.3 Chapter aim | 2 |
| 1.1.4 Epidemiology | 2 |
| 1.1.5 Drug developments | 3 |
| 1.1.6 A personal interest | 4 |
| 1.2 Constructing hepatitis C | 6 |
| 1.2.1 The social construction of disease | 6 |
| 1.2.2 Non-A, non-B hepatitis | 9 |
| 1.2.3 A disease of addiction | 10 |
| 1.2.4 A delayed response | 12 |
| 1.2.5 Pharmaceutical developments | 15 |
| 1.2.6 A public health priority | 16 |
| 1.2.7 Summary | 19 |
| Chapter 2: Living with hepatitis C: a review of the literature | 22 |
| 2.1 Introduction | 22 |
| 2.2 Search strategy | 22 |
| 2.3 The literature review | 23 |
| 2.3.1 Patient-reported outcome measures | 23 |
| 2.3.2 HRQoL in individuals living with HCV | 25 |
| 2.3.2.1 Causal investigation: virus-related factors | 25 |
| 2.3.2.2 Causal investigation: extra-hepatic manifestations of HCV | 26 |
| 2.3.2.3 Causal investigation: host-related factors | 28 |
| 2.3.2.4 Causal investigation: stigma | 30 |
| 2.3.3 HRQoL pre-treatment | 31 |

| | |
|--|-----------|
| 2.3.4 HRQoL during treatment | 32 |
| 2.3.4.1 <i>The early years</i> | 32 |
| 2.3.4.2 <i>The arrival of the DAAs</i> | 32 |
| 2.3.5 HRQoL post-treatment | 34 |
| 2.3.5.1 <i>Limitations and weaknesses</i> | 35 |
| 2.3.6 A different paradigm | 36 |
| 2.3.7 Diagnosis | 37 |
| 2.3.8 The lived experience of HCV | 39 |
| 2.3.8.1 <i>Fatigue</i> | 39 |
| 2.3.8.2 <i>Onward transmission</i> | 40 |
| 2.3.8.3 <i>Impact on PWID</i> | 41 |
| 2.3.8.4 <i>Stigma</i> | 45 |
| 2.3.9 The experience of HCV treatment | 48 |
| 2.3.9.1 <i>Barriers and facilitators</i> | 48 |
| 2.3.9.2 <i>Side-effects</i> | 49 |
| 2.3.9.3 <i>Social isolation</i> | 52 |
| 2.3.9.4 <i>Coping during treatment: resilience and support</i> | 52 |
| 2.3.9.5 <i>The persistence of side-effects</i> | 54 |
| 2.4 Discussion | 54 |
| 2.4.1 The limitations of quantitative PROMs | 54 |
| 2.4.2 The value of qualitative insights | 56 |
| 2.4.3 A significant gap | 58 |
| 2.4.4 Research questions | 59 |
| Chapter 3: Methodology and methods | 60 |
| 3.1 Introduction | 60 |
| 3.2 Methodology | 61 |
| 3.2.1 A qualitative approach | 61 |
| 3.2.2 Ontology and epistemology | 61 |
| 3.3 Phenomenology | 63 |
| 3.3.1 Phenomenologies | 63 |
| 3.3.2 Husserl | 64 |
| 3.3.2.1 <i>Intentionality</i> | 64 |
| 3.3.2.2 <i>Bracketing</i> | 65 |

| | |
|--|----|
| 3.3.3 Heidegger | 67 |
| 3.3.3.1 Heidegger: lost in translation? | 69 |
| 3.3.4 Schütz and social phenomenology | 70 |
| 3.3.4.1 Bracketing revisited | 72 |
| 3.3.4.2 A research method | 73 |
| 3.4 Methods | 74 |
| 3.4.1 Sampling | 74 |
| 3.4.1.1 Maximum variation sampling | 74 |
| 3.4.1.2 Inclusion and exclusion criteria | 76 |
| 3.4.1.3 Sample size | 77 |
| 3.4.1.4 A note on saturation | 77 |
| 3.4.2 Data generation: interviews | 79 |
| 3.4.2.1 Semi-structured interviews | 80 |
| 3.4.2.2 Piloting | 81 |
| 3.4.2.3 Consideration of other data collection methods | 82 |
| 3.4.3 A longitudinal aspect | 82 |
| 3.4.4 Recruitment process | 83 |
| 3.4.4.1 Payment for participation | 85 |
| 3.4.5 Data management and analysis | 85 |
| 3.4.5.1 Transcription | 85 |
| 3.4.5.2 Thematic analysis | 86 |
| 3.4.5.3 Social phenomenology and thematic analysis | 87 |
| 3.4.5.4 Identifying themes | 88 |
| 3.4.5.5 Trustworthiness and rigour | 90 |
| 3.4.6 Ethical considerations | 91 |
| 3.4.6.1 Recruitment | 91 |
| 3.4.6.2 Informed Consent | 91 |
| 3.4.6.3 Risk of harm to participants | 93 |
| 3.4.6.4 Confidentiality | 94 |
| 3.4.6.5 Researcher safety | 95 |
| 3.4.7 Summary | 95 |

Chapter 4: Positioning hepatitis C 96

| | |
|--|----|
| 4.1 Introduction | 96 |
| 4.2 Diagnosis | 97 |
| 4.2.1 Starting points | 97 |
| 4.2.2 A contextual diagnosis: drug use | 98 |

| | |
|---|------------|
| 4.2.3 A contextual diagnosis: co-morbidities | 100 |
| 4.2.4 The influence of treatment | 102 |
| 4.2.5 Re-evaluation of life: alcohol | 103 |
| 4.2.6 Re-evaluation of life: drugs | 105 |
| 4.3 An illness continuum | 106 |
| 4.3.1 Feeling fortunate | 106 |
| 4.3.2 The disparity of access | 109 |
| 4.3.3 A continuum of merit | 112 |
| 4.3.4 Theme summation | 113 |
| Chapter 5: Beyond a physical burden | 115 |
| 5.1 Introduction | 115 |
| 5.2 A physical affliction? | 116 |
| 5.2.1 Fatigue | 116 |
| 5.2.2 A disproportionate focus | 117 |
| 5.3 An emotional illness | 118 |
| 5.3.1 Always on my mind | 118 |
| 5.3.2 Onwards transmission | 119 |
| 5.3.3 Stigma | 121 |
| 5.3.3.1 <i>Theoretical basis</i> | 121 |
| 5.3.3.2 <i>Felt stigma</i> | 122 |
| 5.3.3.3 <i>Hepatitis C and injecting drug use</i> | 123 |
| 5.3.3.4 <i>Hepatitis C and HIV/AIDS</i> | 125 |
| 5.3.3.5 <i>Managing a discreditable identity</i> | 126 |
| 5.3.3.6 <i>Enacted stigma</i> | 129 |
| 5.3.3.7 <i>An unexpected response</i> | 132 |
| 5.3.3.8 <i>Covert enacted stigma</i> | 133 |
| 5.4 Support | 135 |
| 5.4.1 Family and friends | 135 |
| 5.4.2 Peer support | 135 |
| 5.5 Discussion | 137 |
| 5.5.1 Theme summation | 137 |

| | |
|--|------------|
| 5.5.2 Addressing stigma | 138 |
| Chapter 6: Reconstructing uncertainty | 140 |
| 6.1 Introduction | 140 |
| 6.1.1 Chapter aim | 140 |
| 6.1.2 Uncertainty in illness theory | 141 |
| 6.2 The antecedents of uncertainty in HCV | 141 |
| 6.2.1 Uncertainty at diagnosis | 141 |
| 6.2.2 Uncertainty of acquisition | 142 |
| 6.2.3 The effects of HCV | 143 |
| 6.2.4 A familiar refrain | 144 |
| 6.3 The certainty of interferon | 145 |
| 6.3.1 An arduous certainty | 146 |
| 6.3.2 Confirmatory experience | 148 |
| 6.4 The uncertainty of interferon-free therapies | 151 |
| 6.4.1 A nebulous grasp | 151 |
| 6.4.2 Suspicion and scepticism | 153 |
| 6.4.3 Conflict | 156 |
| 6.5 Discussion | 157 |
| 6.5.1 A return to theory: appraisal and coping with uncertainty | 157 |
| 6.5.2 Theme summation | 158 |
| Chapter 7: The lived experience of interferon-free treatments for hepatitis C | 160 |
| 7.1 Introduction | 160 |
| 7.1.1 The participants | 161 |
| 7.1.2 A shifting landscape | 161 |
| 7.2 Theme: expectations and realisations | 164 |
| 7.2.1 Interferon's influence | 164 |

| | |
|---|------------|
| 7.2.2 Side-effects | 167 |
| 7.2.3 Practicalities | 171 |
| 7.2.4 Theme summation | 173 |
| 7.3 Theme: An honour and a pleasure | 174 |
| 7.3.1 A positive experience | 174 |
| 7.3.2 Guilt | 177 |
| 7.3.3 Theme summation | 181 |
| 7.4 Theme: Treatment needs | 181 |
| 7.4.1 Support: existing support networks | 181 |
| 7.4.2 Healthcare professionals | 183 |
| 7.4.3 Perspectives on the value of support | 185 |
| 7.4.4 Searching for efficacy: hunting for side-effects. | 188 |
| 7.4.5 The importance of results | 190 |
| 7.4.6 Feeling better | 192 |
| 7.4.7 Theme summation | 193 |
| 7.5 A nonconforming case | 193 |
| 7.5.1 The case of Gary | 193 |
| 7.6 Discussion | 198 |
| 7.6.1 The relationship of themes | 198 |
| Chapter 8: Discussion | 202 |
| 8.1 Introduction | 202 |
| 8.1.1 A brief overview | 202 |
| 8.1.2 Chapter aim | 203 |
| 8.2 Addressing the research questions | 203 |
| 8.2.1 Question one | 204 |
| 8.2.1.1 <i>Familiarity</i> | 204 |
| 8.2.1.2 <i>Treatment rationing</i> | 205 |
| 8.2.2 Question two | 208 |

| | |
|--|------------|
| 8.2.2.1 Theories of chronic illness | 208 |
| 8.2.2.2 Chronicity within the themes | 209 |
| 8.2.3 Question three | 211 |
| 8.2.3.1 The legacy of interferon | 211 |
| 8.2.3.2 A cultural lag | 211 |
| 8.3 Limitations of the study | 212 |
| 8.3.1 Personal limitations | 212 |
| 8.3.2 Methodological limitations | 214 |
| 8.4 Implications of the study | 216 |
| 8.4.1 Implications for policy | 216 |
| 8.4.2 Implications for treatment delivery | 217 |
| 8.4.3 Implications for practice | 218 |
| 8.5 Recommendations | 219 |
| 8.5.1 Recommendations for policy | 219 |
| 8.5.2 Recommendations for future research | 220 |
| 8.5.3 Recommendations for clinical practice | 221 |
| 8.6 Concluding remarks | 222 |
| 8.6.1 A personal reflection | 222 |
| 8.6.2 Thesis contribution. | 223 |
| References | 225 |
| Appendices | 259 |
| Appendix A - Publications resulting from this thesis to date | 259 |
| Health-related quality of life for individuals with hepatitis C: a narrative review. <i>Int J Drug Policy</i> , 26(10), 936-949 | 260 |
| The lived experience of interferon-free treatment for hepatitis C: a thematic analysis. <i>Int J Drug Policy</i> , 38(1), 21-28 | 273 |
| Appendix B - Literature search strategies | 281 |
| Appendix C - Interview schedules | 284 |
| Appendix D - Patient information sheet | 291 |

List of Tables and Figures

| | |
|--|-----|
| Table 1: HRQoL in individuals with HCV | 25 |
| Table 2: HRQoL in individuals with HCV who achieve SVR | 34 |
| Table 3: Maximum variation sample: target & actual numbers recruited | 78 |
| Table 4: Biographical information for participants in longitudinal study | 162 |
| Table 5: Four treatment regimens taken by the participants | 163 |
| Table 6: Quantitative literature search strategy | 282 |
| Table 7: Qualitative literature search strategy | 283 |
| Figure 1: Treatment experience themes and subthemes | 198 |

Abbreviations

| | |
|-------|---|
| AASLD | American Association for the Study of Liver Disease |
| AIDS | Acquired immune deficiency syndrome |
| ALT | Alanine aminotransferase |
| CFS | Chronic fatigue syndrome |
| CMS | Centres for Medicare and Medicaid Services |
| DAA | Direct-acting antiviral |
| EASL | European Association for the Study of the Liver |
| ELPA | European Liver Patients Association |
| EQ-5D | EuroQol five dimensions questionnaire |
| EU | European Union |
| HAART | Highly active antiretroviral therapy |
| HCV | Hepatitis C virus |
| HIS | Healthcare Improvement Scotland |
| HIV | Human immunodeficiency virus |
| HQLQ | Hepatitis quality of life questionnaire |
| HRQoL | Health-related quality of life |
| IPA | Interpretive Phenomenological Analysis |
| LGBT | Lesbian, gay, bisexual and transgender |
| NHS | National Health Service |
| PROM | Patient-reported outcome measure |
| PWID | People who inject drugs |
| PWUD | People who use drugs |
| RCT | Randomised controlled trial |
| REC | Research ethics committee |
| SF-36 | Short-form 36 health survey |
| SMC | Scottish Medicines Consortium |
| SVR | Sustained virological response |
| TasP | Treatment as prevention |
| WHO | World Health Organisation |

Chapter 1

Why hepatitis C, and why now?

1.1 Introduction

1.1.1 Thesis aim and rationale

This thesis concerns the experience of individuals living with the hepatitis C virus (HCV). Whilst a noteworthy corpus of research already exists in this field, the majority of published works were conducted during an era when treatment of the disease was renowned for its prolonged, laborious, and often unsuccessful nature, and options for those infected were limited. In contrast, this thesis takes as its backdrop the significant advances which have occurred, and which continue to occur, in the treatment of the disease in recent years. These therapeutic advances have been much vaunted in the scientific and popular press, celebrated as a revolution in the fight against the disease, and heralded as a new era of treatment (Bertino *et al*, 2016). It is this changing landscape of HCV, this ‘new era’ of therapy, which provides this study’s rationale for the timely re-examination of the lived experience of HCV.

The thesis is based on an empirical study involving qualitative interviews with 20 individuals living with HCV in Edinburgh, Scotland. Through a thematic analysis of the participants’ narratives, it seeks to provide contemporary insights into the experiences of living with HCV in this new era of therapy, in addition to exploring the experience of undertaking a period of HCV treatment with these novel drugs. It is on the basis of these insights and explorations that the importance of considering the lived experience of HCV within policy and practice will be demonstrated.

1.1.2 Thesis structure

The thesis adopts a conventional structure. This introductory chapter aims to set the research into a wider context, focusing on the global magnitude of the HCV problem. It considers how the construction of HCV as a worldwide public health priority has gained authority in recent years, confronting prevailing understandings of HCV as a disease primarily associated with drug use and addiction. It argues that the impetus for the much celebrated developments in treatment has been largely shaped by socio-

cultural, economic and political agendas, rather than an approach which primarily seeks to protect and treat those most affected by the virus. The chapter provides some social historical background to the subsequent literature review in chapter two, which focuses on the experience of illness from the patient perspective, critiquing the results of both quantitative and qualitative patient-reported outcome measures for HCV. This goes on to identify the significant gap in the literature which this thesis aims to address, and states the research questions which shape and direct the empirical work. Chapter three builds on this foundation, and describes the methodology and methods employed, asserting the ontological, epistemological and theoretical underpinnings of the endeavour, and giving a detailed account of the specifics of data collection and analysis. Following this are four chapters of findings. Chapters four to six each focus on one of the main themes evident within the data, exploring the lived experience of HCV. Chapter seven stands apart from the main body of the thesis, and specifically focuses on the experience of interferon-free HCV treatment. Chapter eight then considers these findings as a whole, and discusses their meaning in light of the research questions posed. The thesis draws to a close by considering the implications of this work for policy, treatment delivery and clinical practice.

1.1.3 Chapter aim

Evidently, the advances in drug therapy which provide the rationale for this study did not occur in a vacuum, and this first chapter aims to supply some background as to how the construction of HCV as a global public health priority has gained increasing authority (World Health Assembly, 2016). It begins by describing the scale of the HCV epidemic, and providing further detail of the pharmacological advances in HCV treatment which have arrived in clinical practice over the last five years. My personal connection to the study is then briefly considered. The bulk of this chapter concentrates on placing the pharmacological advances within their historical, socio-cultural, economic and political context by tracing how HCV has been constructed and reconstructed as a disease of addiction and a public health priority.

1.1.4 Epidemiology

Worldwide, it is estimated that over 185 million individuals are living with HCV (Mohd Hanafiah, Groeger, Flaxman and Wiersma, 2013). Injecting drug use is the cause of a

substantial proportion of the global burden of HCV disease, with injecting drug use-attributable HCV highest in high-income nations (Degenhardt *et al*, 2013; Degenhardt *et al*, 2016). Within the UK, the most recent national estimates suggest around 214,000 individuals are infected, of which approximately 36,700 reside in Scotland (Public Health England, 2015). This includes an estimated 5,234 in the NHS Lothian Health Board area (Health Protection Scotland, 2015). Of those who are living in Scotland, approximately 39% are unaware of their HCV positive status, and of those who have been diagnosed, the latest figures estimate only 28% attended a specialist centre for treatment and care in 2014 (Public Health England, 2015).

1.1.5 Drug developments

Recent years have witnessed a rapid evolution in the treatment available for people living with HCV in Scotland. Until 2011, the treatment for this blood-borne viral infection had been stubbornly based around a drug called interferon- α (hereafter referred to as interferon), a notoriously unpleasant immunomodulating agent, with an extensive catalogue of both physical and neuropsychiatric side-effects (Manns, Wedemeyer and Cornberg, 2006). The pegylation of interferon¹, plus its combination with the nucleoside analogue ribavirin, led to the dual therapy standard of care for chronic HCV which endured throughout the 2000s and into the early part of this decade. These drugs needed to be taken for up to 48 weeks, and achieved sustained virological response (SVR) rates which could be described as mediocre at best. Only approximately 40-50% of those with HCV genotype 1² attained a cure (Fried *et al*, 2002).

The autumn of 2011 saw the approval of two new HCV drugs for use in clinical practice: boceprevir (Scottish Medicines Consortium [SMC], 2011a) and telaprevir (SMC, 2011b), signalling the start of a wave of new medications whose mechanism of action directly inhibited HCV viral replication, and which became known appropriately

¹ A chemical modification giving the drug greater stability and in vivo activity (Foster, 2010).

² HCV exhibits substantial variability within its viral genome, allowing the distinction of separate genotypes and multiple subtypes within each genotype class (Zein, 2000). Genotypic prevalence varies around the world, with genotype 1 being the most common strain overall worldwide, and genotypes 1 and 3 constituting the majority of infection within the UK (Messina *et al*, 2015).

as direct-acting antivirals (DAAs). These drugs were originally added into the existing treatment regimen of pegylated-interferon and ribavirin. However, swift developments over the space of a few years resulted in the advent of new DAAs which no longer required the interferon backbone (Pawlotsky, Feld, Zeuzem and Hoofnagle, 2015a). These interferon-free therapies have drastically shortened the length of treatment required to twelve weeks or less; report a considerable reduction in side-effects compared to interferon-based regimens; and have radically improved SVR rates to over 90% (Asselah, Boyer, Saadoun, Martinot-Peignoux and Marcellin, 2016).

The arrival of interferon-free regimens for the treatment of HCV has been heralded worldwide as a medical triumph, and described as the dawn of a new era in HCV therapy (Chung and Baumert, 2014). To underline this fact, *The New England Journal of Medicine* published no fewer than ten original articles and four associated editorials within the space of only a few months in 2014 documenting the progress made in the field of interferon-free HCV therapies (Pockros, 2014). It is worth noting at this point that, despite these medications achieving remarkable results, their worldwide use has been hampered by their considerable costs and ensuing debates about their cost-effectiveness (Najafzadeh *et al*, 2015). As a result, HCV treatment guidelines in Scotland recommended both interferon-free and interferon-based therapies during the timeframe of this study, subject to specific criteria being met (Healthcare Improvement Scotland [HIS] and National Health Service [NHS] National Services Scotland, 2015a). The costs of these drugs will be discussed further in due course (section 1.2.5).

1.1.6 A personal interest

It was shortly prior to the dawn of these much celebrated developments in treatment that I first began work as a HCV clinical nurse specialist in 2009. Prior to this, I had worked within the dual specialities of infectious diseases and genitourinary medicine as a staff nurse. However, the HCV nurse specialist role allowed me to narrow my focus to this particular cohort of patients, and concentrate my attentions on their specific set of healthcare needs. The role ignited my curiosity into a viral infection that I had perhaps seen as less interesting and less weighty than more media-friendly infections such as the human immunodeficiency virus (HIV).

The work proved both enjoyable and often emotionally draining. The prolonged nature of HCV treatment at the time, and the laborious pre-treatment work-up patients were required to engage with, provided time for close ties to be formed and durable therapeutic relationships built. Nursing care extended beyond the notional 'HCV nurse specialist' title, encompassing emotional and practical support with worries that eclipsed the viral infection, and proved a higher priority for the individuals concerned. Days were filled identifying and initiating appropriate person-centred approaches to help address drug use, alcoholism, homelessness, financial adversity, immigration status, domestic abuse as well as various physical and psychological comorbidities. Referrals were made, followed-up, remade and pursued. My clinics moved out of the hospital and into the community, to needle exchanges, harm reduction services and prisons, and the professional relationship and bond with my patients grew.

As the new era of HCV treatment dawned, international conferences and hepatology journals became filled with data announcing rising SVR rates, reduced treatment length and improved adverse event profiles. Whilst these developments were clearly welcomed, the pharmacological progresses seemed to side-line and drown out the individual patient stories that I had come to know so well. As the refrain that HCV treatment was getting 'easier' flourished, the individuals with the disease seemed to matter less. When the opportunity arose for me to undertake a doctorate degree, my instinct was to honour these individuals, and the disarming honesty and candour with which they had allowed me into their lives over the years, and focus on their stories, their experiences: their voice. I wanted to know how these developments in treatment, these medical triumphs, were being experienced and understood by the very people who were living with the virus.

To begin, however, it is necessary to provide some wider context for this work, and address how the disease of HCV has been socially constructed and reconstructed over time, underscoring the constructivist epistemology which guides this undertaking (which itself will be justified within chapter three). By tracing the social history of HCV through the examination of key policy documents and associated scientific literature, the factors which have contributed to its prioritisation on the world stage can be

examined, and the present study which is concerned with the contemporary experience of being HCV positive, can be placed within an historical, socio-cultural, economic and political landscape.

1.2 Constructing hepatitis C

1.2.1 The social construction of disease

The essential ability and need to categorise the world is fundamental and intricately embedded into our lives: to classify is human (Bowker and Star, 1999). Formal and informal systems of classification are interwoven throughout society, and assert an indisputable and inescapable influence, establishing social and moral order. Within the field of health and illness, the reductionist biomedical model of medicine has historically maintained a dominant role in the classification of disease. However, this paradigm has been increasingly challenged and critiqued in recent decades for its failure to locate disease and illness within its social, environmental and cultural setting (Nettleton, 2006). In contrast, numerous medical sociologists have engaged in inquiries concerning the socio-cultural dimensions of disease for many years, with social constructionism emerging as a dominant theoretical perspective underpinning their work (Lupton, 2007). Within this paradigm, disease is the result of social and interpretive processes which transform collections of symptoms into discrete entities, placing disease classification not merely within the realms of anatomy and traditional medical authority, but within wider social, temporal and cultural contexts. As Rosenberg (1989) asserted, disease does not exist until we have agreed that it does.

The process by which a particular condition becomes categorised as a disease, and how that disease is shaped and understood, is therefore influenced by social, cultural and political factors. Consider the case of Chronic Fatigue Syndrome (CFS), a condition of unknown aetiology characterised by unexplained and persistent fatigue coupled with a marked decline in social functioning (Richman, Jason, Taylor and Jahn, 2000). Historically termed neurasthenia, this condition was originally framed as a somatic disease of the nervous system, mainly affecting the highly educated upper classes, who engaged in prolonged and intense intellectual work (Lian and Bondevik, 2015). During the twentieth century, organic explanations were gradually replaced by more psychogenic ones as a biomedical cause remained elusive, and a pejorative

construction of CFS as an inability to cope emerged, shaped by the predominant cultural norms and values of the time (Jason, 2012). CFS became framed derogatively in the media as 'yuppie flu', with sufferers often regarded as malingerers and shirkers of their normative societal roles. Long-term exhaustion was no longer a high-status badge of honour as it had been in the late nineteenth century, but a dubious and contested diagnosis which stigmatised and blamed the sufferer for their apparent weakness and failure in dealing with contemporary society (Lian and Bondevik, 2015). The same cluster of symptoms had been constructed and reconstructed in popular and professional discourse over time, relocating it from a somatic biological disease to a questionable psychogenic syndrome, which ultimately delegitimised the patient experience (Ware, 1992).

A social constructionist approach therefore emphasises how disease is constituted within institutional and cultural traditions, shifting frameworks of knowledge, and relations of power (Conrad and Barker, 2010). However, discussion of disease as a purely socially considered collection of symptoms does not quite ring true. What of biological factors, pathophysiology and diagnostic technologies? The rise of laboratory medicine has moved the traditional locus of disease away from collections of symptoms to the cellular level (Gardner, 2014), making biological explanations for illness increasingly relevant in society, as illustrated by the case of CFS. Timmermans and Haas (2008) note that sociologists often have an aversion for taking biological factors into consideration, standing with their backs to the heart of medicine and studying the social phenomena encircling it. Such authors discuss endemic concerns amongst sociologists that recognition of biological factors implies an automatic devaluation of social factors in the construction of disease. Similarly, in his call for a sociology of diagnosis, Brown (1995) queries why an appreciation of causative biological pathogens must automatically prevent us from grasping the social construction of the resulting conditions. Within a critical-realist perspective, the existence of pathogenic microorganisms is not contested. However, they are not viewed as objects which have fixed and given identities, but rather as entities that gradually come into being as human consciousness and scientific attention are directed towards them. Biological factors and social constructionism are therefore necessarily intertwined. As something becomes defined and measurable, it becomes

clinically actionable and socially, politically and culturally resonant. In other words, what comes to count as disease and the consequences of this *can* be biological, but are always socially produced. As Fraser and Seear (2011) note, disease is a gathering, made by social practices, values and conventions as much as by microbes.

This discussion has particular significance in the case of HCV. The identification of a causative microorganism in 1989 allowed a framing and shaping of the disease, constructing an identity which had political, cultural, economic and social connotations. Hepatitis C does not simply designate an invariant biological reality, but has been created and recreated through the language, practices, social interactions and negotiations which surround it (Nettleton, 2006). The remainder of this chapter draws on the work of Suzanne Fraser and Kate Seear, who analysed HCV from a cultural and social perspective in their book *Making Disease, Making Citizens* (2011), providing powerful insight into how political and social forces have shaped and reshaped the disease. Their work in turn acknowledges the influence of numerous other scholars, notably Annemarie Mol (1999), who argued that constructions of disease are made and remade by multiple processes of constitution, continually iterated rather than singular and immutable. Understandings and constructions of HCV are therefore plural, constituted by the cultural, political and societal contexts in which they are found (Duffin, 2005). As Fraser (2010) remarks, HCV is more than one and less than many.

The relative authorities of multiple disease constructions has significant implications. For example, the reconstruction of HIV/AIDS from a 'gay plague' to a chronic illness during the 1990s remade the cultural perception of people with HIV/AIDS as long-term survivors rather than terminally ill, which in turn resulted in a revision of governmental and community priorities for the support of people with the disease (Paterson, Butt, McGuinness and Moffat, 2006). The cultural meaning of a disease therefore shapes how society responds to it, and powerfully influences the lived experience of those individuals afflicted by the condition (Conrad and Barker, 2010). In order to understand a disease, therefore, the multiple discourses in which it is embedded must be examined.

1.2.2 Non-A, non-B hepatitis

From the 1960s, viral hepatitis was considered to represent two clinically distinct diseases: infectious hepatitis (or hepatitis A) and serum hepatitis (or hepatitis B) which was corroborated by diagnostic technologies available at that time (Pawlotsky *et al*, 2015a). Advances in serological assays during the 1970s allowed the screening of blood donations for both hepatitis A and B. Despite this, a significant percentage of patients continued to be affected by hepatitis following blood transfusions, implying a third form of viral hepatitis could be present (Feinstone, Kapikian, Purcell, Alter and Holland, 1975). This third form was termed non-A, non-B hepatitis, indicating an exclusion of exposure to hepatitis A or B, but acknowledging an awareness that more than one other viral agent was likely to be responsible for this group of infections (Gitnick, 1984). Despite this early work, the biomedical categorisation of the non-A non-B infectious agents remained elusive for well over a decade (Houghton, 2009).

The early construction of HCV disease was therefore indistinct and unclear. It was neither one thing nor the other, an unknown, lumped together with other viral hepatitises yet to be recognised. However, despite its ambiguous identity, the political influence of non-A non-B hepatitis was beginning to be felt. In the USA, the incidence of post-transfusion hepatitis due to non-A non-B was observed to occur significantly more frequently following transfusion of commercially derived blood than following receipt of blood derived from volunteer sources (Purcell, Alter and Dienstag, 1976). This observation contributed to a resolution by the World Health Assembly urging Member States to promote the development of national blood services based on voluntary non-remunerated donations (World Health Assembly, 1975). In addition, reports were emerging of high levels of non-A non-B hepatitis in people who inject drugs (PWID) (e.g. Fielding, Shattock, Doyle and Kelly, 1983), and the gradual integration of the prefixes 'post-transfusion' and 'community acquired' filtered into the non-A, non-B hepatitis discourse (e.g. Sampliner *et al*, 1984). These epithets were value-laden: a passive nosocomial infection versus a disease that had been actively acquired in the community. In applying these prefixes, the social causation of non-A non-B hepatitis was written into its identity, creating a disease which affected individuals who could be labelled as accidental victims (innocent) or warranted

recipients (guilty) (Duffin, 2005). Even prior to being identified and named, the building blocks of HCV disease were being laid down.

1.2.3 A disease of addiction

The identification and description of HCV in 1989 (Choo *et al*, 1989) had significant implications for the disease. Whilst non-A, non-B hepatitis encapsulated a collection of unknowns, the name HCV presented the virus as a singular entity (despite growing awareness of its genetic heterogeneity [Bukh, Miller and Purcell, 1995]), making it specific and allowing a diagnosis. Diagnosis is integral to the system of medicine and the way it creates social order, embodying the time and place when permission is given to be 'ill', and conferring legitimacy on a condition (Jutel, 2009). This legitimacy can entitle the sufferer to compassion and sympathy, however, a diagnostic label can also attract stigma and generate stereotypical perceptions depending how the disease is characterised (Garand, Lingler, Conner and Dew, 2009). In high- and middle-income countries, diagnosis also provides a licence to access resources, support and assistance which may otherwise be unavailable, although in low-income countries where resources and treatment are scarce, the act of diagnosing can be surrounded by considerable ethical dilemmas (Rennie and Behets, 2006). In this case, the identification of HCV also brought practical benefits and meant that donated blood could be effectively screened (Houghton, 2009) and the risks of post-transfusion HCV began to decline significantly in high- and middle-income countries (Donahue *et al*, 1992)³. In the West therefore, the risks of obtaining HCV through blood transfusion faded, and discussion surrounding entitlement to compensation for those who had previously been infected arose (Angelotta *et al*, 2007). The prefixes of 'post-transfusion' and 'community acquired' gradually faded from use in line with the reduced risks of contracting HCV through iatrogenic means. In consequence, the social perception of HCV in Western countries began to focus almost exclusively on those deemed most at risk of spreading and acquiring the infection.

Throughout the 1990s and 2000s, HCV was depicted as a disease of misadventure. It was for those who injected drugs, had rough and unprotected sex, required medical

³ although iatrogenic spread remained (and remains) the most common route of transmission globally (Pawlotsky *et al*, 2015a)

treatment abroad or adorned themselves with tattoos and body piercings. This was no longer a disease you could accidentally contract, it was one you had to go out and actively find. Chief amongst these risks was the intravenous injection of drugs, and prevailing societal understandings towards drug use and PWID became inextricably enmeshed in the construction of HCV. In the same way that negative attitudes towards HIV/AIDS had been associated with negative attitudes towards gay men, so judgements towards HCV and PWID were comparably entwined (Brener and Von Hippel, 2008). For example, intensely negative public attitudes towards opioid substitution therapy for PWID have been aligned with a belief that addiction is self-inflicted (Matheson *et al*, 2014). In much the same way, HCV also became understood as a disease that was the result of the sufferer's irresponsible behaviour rather than ill-fortune. Accounts of stigma and discrimination in relation to HCV were often tenaciously associated with illicit drug use irrespective of the mode of acquisition (Butt, Paterson and McGuinness, 2008; Hill, Pfeil, Moore and Richardson, 2015), and health promotion literature concerning HCV became (and remains) almost exclusively aimed at PWID, often conflating HCV and drug use within the texts, inextricably tying them together (Fraser and Seear, 2011). Hepatitis C, more than ever, became a disease of addiction, and, as such, the social appetite for addressing the epidemic was muted. Further, whilst HIV/AIDS may have benefited from its association with the politically and economically empowered gay community (Fee and Krieger, 1993), HCV had few similarly influential or mobilised groups beating its drum.

The media styling of HCV as 'a silent killer' reinforced the lack of impetus. As Sontag (1979) contended, metaphors are not just evocative figures of speech, they have the power to shape and construct our understanding. A perception of HCV as a silent killer implies the disease is too unpredictable, insidious and complex to be ultimately manageable, tacitly shaping the impression that there is little that can be done (Fraser and Seear, 2011). Silent killers are not often caught. Consider this in relation to the language and metaphor used in other diseases. For example, cancer is something which is battled and can be beaten. The discourse around cancer is rich in military metaphor (Harrington, 2012), galvanising public opinion that a war on cancer is one that ought to be fought, and constructing a disease that can be overcome given

enough resources and time. In contrast, the advance of HCV is silent and undetected until its victory is secured; a disease for which battle is futile.

1.2.4 A delayed response

The construction of HCV as a disease of addiction and one for which little could be done placed it at a distinct disadvantage politically, contributing to a lethargic global policy response at odds with other major communicable diseases. Not until 2010 did the World Health Assembly adopt its first ever resolution on viral hepatitis - WHA 63.18 - acknowledging the global public health problem and calling for a comprehensive approach to prevention and control (World Health Assembly, 2010). As a contribution towards that objective, the World Health Organisation (WHO) published a strategic framework to guide Member States in progressing their national action plans (WHO, 2012) in addition to conducting a survey aimed at gathering country-specific baseline data on hepatitis policies from individual governments (WHO, 2013). The results of this survey revealed a sporadic and erratic global response to HCV, with just 37.3% of the Member States who responded⁴ reporting the existence of a written national strategy or plan focussing exclusively or primarily on viral hepatitis. Furthermore, the response to this report from patient groups, non-governmental organisations, academic institutions and medical associations questioned the accuracy of much of the published governmental data, disputing key claims regarding viral hepatitis prevention and control, and highlighting a lack of engagement between governments and civil society stakeholders (World Hepatitis Alliance, 2014). A further resolution from the World Health Assembly duly followed - WHA 67.6 - calling more forcefully for a comprehensive global strategy in the face of a growing public health problem (World Health Assembly, 2014). However, it was not until 2016, 27 years after the identification of HCV, that the World Health Assembly adopted the Global Health Sector Strategy on viral hepatitis, with the goal of eliminating HCV as a major public health threat by 2030 (World Health Assembly, 2016).

At a European Union (EU) level, the response to HCV has been even more sluggish. In 2007, the European Parliament adopted Written Declaration 0087/2006, calling for

⁴ In total, 126 Member States submitted the survey for a response rate of 64.9% (WHO, 2013).

recognition of HCV as an urgent public health issue (Dičkutė, Bowis, Hughes, Ries and Ulmer, 2006). However, despite including viral hepatitis in its priorities for 2008, the EU agency responsible for disease-specific data collection did not begin enhanced surveillance of HCV within Europe until 2011 (European Centre for Disease Prevention and Control, 2013). Further, the lack of consistent and harmonised surveillance mechanisms within Member States presented concern over the reliability of the data collected, and constituted a significant gap in EU legislation (Ulmer and Hughes, 2013). A further Written Declaration, 0023/2013, calling on more action by the European Parliament in respect to the “urgent public health issue” of HCV (Țicău *et al*, 2013) lapsed in 2014 after failing to gather sufficient signatories, and across Europe a uniform approach to the management of the disease remains absent. Pockets of work continue however, and in 2016 the first high-level European policy summit in relation to HCV took place (Hepatitis B and C Public Policy Association, 2016) resulting in a manifesto in line with the World Health Assembly objective: the elimination of HCV in Europe by 2030.

Whilst a languid international response to HCV can be traced through the exploration of grey literature and key policy documents, a more dynamic national response has been evident in some countries. Within the UK, where most health policy is a devolved matter, the then Scottish Executive declared in 2004 that HCV was one of the most serious and significant public health risks of our generation, and a nationally coordinated and government funded two-phase *Hepatitis C Action Plan* was subsequently initiated in 2006 (Scottish Executive, 2006). The impetus for this vigorous response to HCV came from two main sources: an unusually vocal and determined group of HCV positive individuals whose lobbying instigated a report on HCV by the Scottish Needs Assessment Programme (SNAP, 2000), and a Consensus Statement on HCV which emerged from the Royal College of Physicians in Edinburgh in April 2004 highlighting the growing burden of infection and liver disease on existing services (Scottish Executive, 2005). These documents galvanised a political response to the growing epidemic in Scotland by identifying the prevention of HCV transmission and increasing diagnosis of HCV as their primary objectives. The treatment of those infected was framed as a subordinate consideration. Indeed, on-going injecting drug use was noted as an explicit contra-indication for receiving therapy (Scottish Executive,

2005). As this discourse developed and the Action Plan matured, subsequent improvements in testing, treatment, care and support were implemented from 2008 accompanied by major governmental investment of £43 million over three years (Scottish Government, 2008). In 2011, the *Hepatitis C Action Plan* was incorporated into a new policy framework integrating sexual health and blood borne viruses (Scottish Government, 2011), and remains globally renowned and considered as leading best practice in a national response to tackling and treating HCV (Ulmer and Hughes, 2013).

Despite examples of best practice in specific regions, the overall global response to HCV has been hindered and shackled by cultural perceptions of the disease. The social stigmatisation associated with injecting drug use is not only subjectively internalised by HCV positive individuals (Paterson, Backmund, Hirsch and Yim, 2007), but also tacitly influences decisions by social and healthcare agencies, and sways governmental policy (Room, 2005). Consider the discourse surrounding compensation claims for those iatrogenically infected through blood products. Whilst countries such as Canada, Ireland and the UK eventually allocated compensation and ex gratia payment funds, the response from other nations has been markedly subdued (Angelotta *et al*, 2007). For example, a Written Declaration to the European Parliament in 2011 calling on the need to provide appropriate compensation for victims of infected blood failed to garner support (Rossi, 2011). In contrast, most developed countries implemented a broad range of political and legal responses to the contamination of the blood supply with HIV in the 1980s. More than 20 countries offered financial compensation to people with haemophilia who had contracted HIV through infected blood; health officials in Japan and France were convicted of criminal negligence; and civil lawsuits against suppliers of HIV contaminated blood were adjudicated resulting in blood product suppliers providing financial recompense (Angelotta *et al*, 2007). Once again, whilst HIV benefitted from its association with a politically empowered and vociferous section of the gay community, HCV floundered due to its lack of campaigning voice and intimate association with illegal drug use.

1.2.5 Pharmaceutical developments

At odds with the lethargic and disjointed global political response, the recent developments in the treatment of HCV by the pharmaceutical industry have been framed as a rapid 'medical triumph' and the culmination of successive biomedical advances (Chung and Baumert, 2014). The historical HCV treatment of interferon (and later pegylated-interferon) and ribavirin has been transformed with the advent of the DAA era (Thiagarajan and Ryder, 2015), a therapeutic revolution hailed as truly remarkable given it has occurred less than 25 years since the identification of the virus. There are now numerous combinations of drugs available for HCV treatment, with many more in phase II and phase III clinical trials (Pawlotsky *et al*, 2015a). However, whilst often framed as a progressive succession of discoveries over this time, the advances in HCV treatment have not been as rapid as retrospective accounts suggest. The first DAAs did not arrive in clinical practice until 2011, 22 years after HCV was identified (Thiagarajan and Ryder, 2015). The 'treatment revolution' has therefore only moved out of the laboratory in the last five years, meaning that throughout the 1990s and 2000s a disease which disproportionately afflicts the most disenfranchised sections of society endured an arduous, challenging and lengthy therapy which had a limited efficacy of approximately 40-80% (Thiagarajan and Ryder, 2015). Over approximately the same period of time, some 25 different drugs in six different classes, as well as a variety of fixed dose combination pills, were developed and licensed for the treatment of HIV (Zolopa, 2010), inferring the delays in new therapies emerging for HCV were not solely limited by the virological technologies of the day.

Whilst advances in drug therapy are now encouraging and enabling academic discussion of global HCV eradication (Hagan and Schinazi, 2013), there is a colossal difference between large pharmaceutical companies producing a product that can cure a disease, and afflicted people around the world obtaining the drugs. The high cost of DAAs precludes their use in most infected patients in low- and middle-income countries, and in high-income countries fiscal considerations and insurance provider policies have resulted in selective use (Chung and Baumert, 2014). For example, in America, State Medicaid programmes, which provide healthcare for families and individuals on low incomes and with limited resources, have restricted access to DAAs due to their substantial costs (Canary, Kleven and Holmberg, 2015). In response, the

Centres for Medicare and Medicaid Services (CMS) released a guidance document highlighting restrictions on access to treatment which they deemed were unreasonable (CMS, 2015), however, it remains to be seen what impact this guidance will have. Even in Scotland, a benchmark for excellence in terms of national strategy, the SMC continued to only approve DAAs for restricted use due to financial concerns during the timeframe of this study (e.g. SMC, 2015a). As Nettleton (2006) has noted, a 'medical triumph' is not determined by technological advances, but rather is the outcome of the socio-political struggles that surround technology and its application. Patient groups concur, emphasising the significance of the social aspects of HCV and questioning any assertion that the disease could be brought under control by science alone (World Hepatitis Alliance, 2014).

1.2.6 A public health priority

After languishing as a disease of addiction for over twenty years, why was HCV eventually thrust onto the global public health agenda? What factors served to promote the framing of HCV as a public health priority, and generate sufficient economic impetus to drive the pharmaceutical arms race currently being witnessed? The increasing prevalence of HCV is an obvious rejoinder. However, this had been monitored by the WHO, amongst others, for many years with little sign of momentous change. In 1997, the WHO estimated a global prevalence of approximately 3% with the virus affecting more than 170 million people worldwide (WHO, 1997), a figure which was subsequently revised down to 2.2% by further WHO funded work in 2004 (The Global Burden of Hepatitis C Working Group, 2004). The most recent estimates of disease burden suggest an increase in global seroprevalence from 2.3% in 1990 to 2.8% in 2005, equating to over 185 million infections worldwide, with significant variations between geographic regions (Mohd Hanafiah *et al*, 2013). Early estimates of the global prevalence of HCV have not therefore drastically changed between the late 1990s and more recent assessments, suggesting that the emerging and increasing contemporary discourse of HCV as a global public health emergency is not solely driven by the number of individuals living with the disease. The public health emergency has always been there, yet its public profile was historically subdued. It is necessary therefore to consider other influences which contributed to the social reconstruction and underscoring of HCV as a public health priority.

A strong and persuasive narrative emerges from patient advocacy groups. Initially disparate and isolated, they gradually came together during the first decade of the twenty-first century and mobilised under the World Hepatitis Alliance umbrella, in direct response to the absence of an international public discourse around the disease. In addition to raising the public profile of HCV through originating World Hepatitis Day in 2008, they were also instrumental in demonstrating the need for both World Health Assembly resolutions, advocating and lobbying Member States to adopt the proposals (World Hepatitis Alliance, 2016). Within Europe, the European Liver Patients' Association (ELPA) brought together national liver patient groups from across the continent, successfully influencing the European Parliament's adoption of their Written Declaration in 2007 (Piorkowsky, 2009). A louder and more powerful patient voice had emerged, directly at odds with the dominant perception of HCV patients constructed throughout the previous decades, which had been easy to ignore. Hepatitis C patients were becoming visible and empowered on the international stage, using their collective presence to influence the global health agenda. The recent pharmaceutical advances have themselves spurred further patient advocacy, as disparity of access to new DAAs presents a new banner under which to mobilise (Trooskin, Reynolds and Kostman, 2015).

It is worth briefly considering how patient advocacy groups achieved this dynamic global voice. Fraser and Seear (2011) observed that the model of the 'politically active patient' is inapposite to the majority of individuals affected by HCV in high-income nations, indeed, those with HCV are more commonly cast as PWID risk-takers, framed as lacking in self-control and deemed 'guilty' for their infection (as previously described). Such individuals are positioned as undeserving of patient citizenship, with little connection to community activism and little entitlement to treatment and care (Rhodes, Harris and Martin, 2013). In order to make their voice heard therefore, patient advocacy groups have distanced themselves from 'guilty' distinctions of HCV, aligning more visibly with less culpable or morally questionable individuals who acquired the disease through iatrogenic means⁵ – the 'innocent' parties (Duffin, 2005). This positioning allowed a presentation of HCV positive individuals as victims of an

⁵ For example, consider the much publicised patronage of the *Hepatitis C Trust* by Anita Roddick, who acquired HCV through a blood transfusion during the birth of her son in the 1970s.

unforeseen tragedy, eliciting emotions of sympathy and rightful anger (Seear, Fraser and Lenton, 2010) which carried greater political weight. The advocacy movement speaks for all, but is strategic in how it achieves this.

Patient activism alone is not the whole story, however, as multiple narratives and authorities have served to reconstruct HCV into a global public health priority. Whilst retrospective accounts tend to frame the belated prioritisation of HCV as a result of scientific and political pressure to address health inequalities in marginalised populations (e.g. Wylie, Hutchinson, Liddell and Rowan, 2014), economic motivations were also considerable factors. The early economic discourse around HCV focused on the cost-effectiveness of specific treatments, but lack of certainty around long-term clinical outcomes and questionable efficacy of the drug available at the time made this a particularly inexact science (Koff, 1997; Shiell, Briggs and Farrell, 1994). Slowly, however, a narrative arose concerning the future costs to the healthcare system of HCV sequelae from untreated infections. Early work from Australia in 1998 estimated that the costs of treating chronic hepatitis, cirrhosis, liver failure and hepatocellular carcinoma amongst their population of PWID over the next 60 years could total AUS\$4 billion, and called for urgent action from national policy-makers to forestall this predicted bill (Brown and Crofts, 1998). A wider discourse on disease burden subsequently emerged with assessments of the accumulated costs of HCV-related liver disease in other countries appearing within the literature. Sheerin, Green and Sellman (2003) estimated the accrued costs related to HCV within the PWID cohort in New Zealand to be in the region of NZ\$166-400 million whilst in America the predicted direct medical costs to treat future HCV-related disease was conservatively estimated between US\$6.5-13.6 billion with societal costs adding an additional US\$21.3-54.2 billion over ten years (Wong, McQuillan, McHutchison and Poynard, 2000). Similarly costly forecasts followed from other regions (e.g. Saadany, Coyle, Giulivi and Afzal, 2005; Vandijck *et al*, 2014), with global estimates of the cost of HCV-related disease eventually taking shape (El Khoury, Wallace, Klimack and Razavi, 2012).

The importance of this narrative to contemporary discourse is evident. The published academic literature continues to sound warning sirens at the downstream healthcare costs associated with HCV (Gordon *et al*, 2013; Harris *et al*, 2014), and current

international and national public health policy places the pecuniary burden of HCV disease at its heart. The first WHO guidelines for the care and treatment of people with HCV notes that new treatments have the potential to reduce dramatically the health *and* economic burdens associated with the infection (WHO, 2014) whilst the foreword to a recent account of HCV in the UK states that it “*highlights the work that still needs to be done to curtail the increasing burden of end stage liver disease and liver cancer caused by hepatitis C infection*” (Public Health England, 2015, p.5). Echoes of this narrative are also found in professional guidance for healthcare practitioners. Both the American Association for the Study of Liver Disease (AASLD, 2015) and the European Association for the Study of the Liver (EASL, 2015) have previously advocated prioritising the treatment of those individuals with a greater degree of liver damage (Metavir stage F3 and F4) where resources are limited. Whilst distributive justice in terms of liver disease prioritises those most at risk of immediate ill health, it also implicitly prioritises those who are more likely to incur downstream healthcare costs due to the complications of cirrhosis and hepatocellular carcinoma (Tapper *et al*, 2016). This is more salient when the evidence suggesting *earlier* treatment for HCV, that is, treatment of those with minimal fibrosis, offers a better response to therapy and improved long-term survival (e.g. Jézéquel *et al*, 2015).

1.2.7 Summary

As previously stated, in order to understand a disease and society’s responses to it, the discourses in which it is embedded need to be examined. A social constructionist critique of HCV demonstrates how the disease is more than simply the name given to a collection of biological pathogens: it is an evolving and dynamic social entity that invokes certain logics of treatment and care. This summary of the socio-cultural and political history of HCV has drawn on diverse bodies and sources of literature from over 40 years. It has done so in order to situate the disease within its wider context, and provide the biomedical history of HCV disease with a complementary interpretation which resonates with the theoretical foundations of this thesis. Social, cultural, political and economic forces have contributed to shaping and reshaping understandings of HCV which are replete with assumptions and opinions about what the disease means and what it merits.

Since its identification, HCV has been predominately shaped within high-income countries as a disease entwined with illicit drug use, tainted by the stigma, discrimination and negative societal judgements that this practice attracts. Treatment of those most affected by the disease has also been primarily about engaging with a population of largely demonised PWID, individuals deemed guilty for their infection and with little claim to therapeutic citizenship. These constructions permitted a restrained political response to the growing epidemic, until an increasing awareness amongst policy- and decision-makers of the predicted financial burden that HCV threatens globally necessitated a shift in the public discourse from a disease which affected a marginalised and socially stigmatised group, to one which was relevant to wider sections of society. To address the predicted financial burden of HCV, society's understanding of it needed to be refocused, disentangling its identity from illicit drug use and shaping a predominant understanding of HCV as a public health priority. Hepatitis C has been reconstructed within the global arena as a disease with broader social and economic implications, galvanising governmental responses and creating an environment ripe for pharmaceutical investment. The mobilisation of the response to HCV has appeared in line with the gradual movement of a broader public health narrative to centre stage. This narrative focuses on the burden of disease and its implications for health services and service providers rather than the physical and emotional costs to individuals and their families. A disease deemed to affect primarily PWID has been remade in terms of something wider sections of society can empathise with: money. Whilst this focus on HCV as a public health priority has stimulated the current momentum to address the disease, there is a danger that it may also serve to silence personal experience and individual suffering.

Within this chapter, I have endeavoured to demonstrate how socio-cultural, political and economic forces have contributed to the construction and reconstruction of HCV over the last 40 years in order to situate the disease and this thesis within its temporal context. In doing so, I have composed a narrative situated decisively within the Western world, and of relevance to the local situation in Scotland, as the global response to HCV and its assembly as a public health priority have been driven by

wealthier industrialised nations⁶. This discussion provides context to the developments in drug therapy which provide the rationale for this thesis, and also begins to offer justification for the focus given to the patient experience and understanding of the disease. As a nurse, understanding the meanings, implications and consequences of HCV from the point of view of the people most affected, provides insights which can only enhance and develop better clinical care.

⁶ The areas of highest HCV prevalence are found in Central and Eastern Asia, North Africa and sections of the Middle East (Mohd Hanafiah *et al*, 2013) where resources are limited and strategies to address the epidemic are correspondingly embryonic. It remains to be seen how the HCV public health agenda, driven by resource-rich and globally influential countries, manifests itself in the poorer regions of the world where the disease is most widespread.

Chapter 2

Living with hepatitis C: a review of the literature

2.1 Introduction

Having considered the wider socio-cultural, economic and political contexts in which this thesis is situated, the aim of this chapter is to review the extant body of literature focusing on the perspective of those living with HCV. This is achieved through the examination of studies which have reported either quantitative or qualitative patient-reported outcome measures. Firstly, the quantitative assessment of health-related quality of life in individuals with HCV is presented, revealing a significant decrement compared to population norms. This body of work also investigates the multifactorial underlying cause, and the effects of HCV treatment. Secondly, the qualitative literature pertaining to the lived experience of HCV is explored, and the limitations of the quantitative approach critically considered. An argument is then made that qualitative research in this area not only aids the interpretation of the quantitative data, but offers deeper and more nuanced insights into a complex phenomenon⁷. This discussion also highlights the significant gap in knowledge which this thesis aims to fill, and ends by stating the research questions which guide the empirical work described in the subsequent chapters.

2.2 Search strategy

The search strategy focused on seven medical, sociological, psychological and nursing databases: Medline; CINAHL; Embase; Cochrane Library; JBI COnNECT+; PsycINFO and ASSIA. Two separate search strategies were developed to identify both quantitative and qualitative reports. For quantitative papers, comparable search terms for 'hepatitis C', 'health-related quality of life' (including common abbreviated forms) and 'patient reported outcomes' were used, accounting for variation in the subject index terms specific to each search engine. For qualitative papers, comparable search terms for 'hepatitis C', 'quality of life' or 'life experience', and 'qualitative research' or 'interview' were used, again accounting for variation in specific subject index terms⁸.

⁷ A published version of this literature review can be found in appendix A.

⁸ The term 'quality of life' is used more generally within the qualitative literature than the more specific 'health-related quality of life'.

In order to obtain papers that provided a detailed historical and contextual view as well as giving contemporary relevance, databases were searched to the extent of their temporal limits, preceding the publication announcing the isolation of HCV (Choo *et al*, 1989) in most cases⁹.

The quantitative search strategy used the following initial inclusion/exclusion criteria: inclusion criteria were adult participants, an English language abstract, and specific quantitative HCV health-related quality of life data provided. Excluded papers were those dealing solely with other liver disease aetiologies, and papers concentrating on those undergoing haemodialysis or liver transplantation. These articles primarily described the impact of those specific interventions which is not the focus of this thesis. The inclusion criteria for the qualitative arm were as follows: adult participants, an English language abstract, 'life experience' focus and qualitative data reported. Exclusion criteria remained the same as for the quantitative search strategy. Both observational and interventional studies were included, as were reviews at this initial stage. Duplicate entries for the same article appearing in multiple search engines were removed.

The remaining articles were retrieved, and the reference lists examined for any further studies which had not been identified to date. Once complete, review articles were then excluded as primary data sources. Data were extracted from the remaining studies using a data extraction sheet which identified the author(s), date and source of publication, study design, key findings, limitations and recommendations. Using these data, key, dominant themes were identified for each research paradigm, which provided the foundation for the formulation of results and the synthesis of a coherent narrative.

2.3 The literature review

2.3.1 Patient-reported outcomes measures

Objective measures of patient outcome are of clear importance within healthcare. However, they do not necessarily include or align with the benefits or most pressing

⁹ Appendix B demonstrates the initial results of the search strategies for each paradigm.

concerns perceived by the patients themselves. With the historical move from a disease-centred model of medicine to a more biopsychosocial paradigm, a focus emerged on not only the biomedical decrements of illness and curative benefits of treatment, but also the experience of illness and treatment from the patient perspective. Increasingly, this experiential focus is being given central importance in the planning of future healthcare improvements (e.g. Scottish Government, 2010), and in the licencing of new medications (Food and Drug Administration, 2009). In addition, an understanding of the patient experience of illness and treatment can also inform clinical practice, aiding interaction and communication with patients and clients on a one-to-one basis (Wu and Snyder, 2012).

Insights into the patient experience of illness and treatment are gained through patient-reported outcome measures (PROMs), an umbrella term used to encompass any report coming directly from a patient about their health condition and treatment. PROMs can therefore be both quantitative and qualitative in nature, although are most frequently reported using data from quantitative self-completed questionnaires. These questionnaires are often specific to a particular symptom such as fatigue (e.g. Fatigue Severity Scale [Krupp, LaRocca, Muir-Nash and Steinberg, 1989]) or pain (e.g. Brief Pain Inventory [Cleeland and Ryan, 1994]), both of which have obvious benefits as these events are generally unobservable and/or unquantifiable from the clinician's perspective. More broadly, however, some tools have been developed to assess multiple health concepts, incorporating physical, emotional and social domains, to provide a multidimensional construct of an individual's health-related quality of life¹⁰ (HRQoL). These quantitative tools can be generic, assessing the HRQoL across patients living with a variety of conditions, or validated in more condition-specific populations.

Health-related quality of life within HCV is most recurrently measured by the Short-Form (SF)-36 Health Survey (Ware and Sherbourne, 1992). This generic self-administered questionnaire consists of 36 items divided into eight domains: physical functioning; role – physical; bodily pain; general health; vitality; social functioning; role

¹⁰ This is still a loosely-defined term, used to distinguish between aspects of life affected by disease or treatment for disease, and those broader quality of life issues such as access to green space within towns and cities (Fayers and Machin, 2007).

– emotional and mental health. Of these, vitality, general health, physical functioning and social functioning are thought to be where the impact of HCV is most pronounced (Speigel *et al*, 2005). These domains can then be aggregated into two summary scores: physical component summary and the mental component summary. This tool has been validated in various condition-specific patient populations, and can also be compared to population norms (Foster, 2009). A supplemented HCV-specific version of this tool is also employed within the literature (the Hepatitis Quality of Life Questionnaire [HQLQ] [Bayliss *et al*, 1998]) but as Foster (2009) notes, whilst this has the advantage of capturing disease-specific data, a more generic tool allows cross-disease comparison. Whilst these tools are the most common, there is no overriding consensus or standardization on their exclusive use within HCV, and other tools also appear within the literature, for example the EQ-5D (Vera-Llonch *et al*, 2013) and the WHOQOL-BREF (Fábregas *et al*, 2013), whilst new instruments continue to be developed, evaluated and validated (e.g. Anderson *et al*, 2014; Armstrong *et al*, 2016).

2.3.2 HRQoL in individuals living with HCV

2.3.2.1 Causal investigation: virus-related factors

The quantitative literature demonstrates HCV positive individuals have reduced HRQoL in comparison to healthy controls or population norms (table 1) and goes onto investigate and debate the underlying cause.

| Author and Year | | Bayliss <i>et al</i> (1998) | Foster <i>et al</i> (1998) | Ware <i>et al</i> (1999) | Borkovsky <i>et al</i> (1999) | Bianchi <i>et al</i> (2000) | McHutchison <i>et al</i> (2001) | Miller <i>et al</i> (2001) | Kramer <i>et al</i> (2002) | Córdoba <i>et al</i> (2003) | Gallagos-Orozco <i>et al</i> (2003) | Fleming <i>et al</i> (2004) | Dalgard <i>et al</i> (2004) | Kang <i>et al</i> (2005) | Hollander <i>et al</i> (2006) | Pojoga <i>et al</i> (2006) | Borkovsky <i>et al</i> (2007) | Kallman <i>et al</i> (2007) | Helbling <i>et al</i> (2008) | Snakos <i>et al</i> (2010) | Kuwashiro <i>et al</i> (2014) | Strauss <i>et al</i> (2014) | Matsushita <i>et al</i> (2014) |
|-----------------|--------------------|---|----------------------------|--------------------------|-------------------------------|-----------------------------|---------------------------------|----------------------------|----------------------------|-----------------------------|-------------------------------------|-----------------------------|-----------------------------|--------------------------|-------------------------------|----------------------------|-------------------------------|-----------------------------|------------------------------|----------------------------|-------------------------------|-----------------------------|--------------------------------|
| n = | | 157 | 116 | 324 | 704 | 126 | 912 | 95 | 200 | 160 | 157 | 299 | 199 | 371 | 147 | 71 | 1144 | 201 | 833 | 190 | 175 | 134 | 228 |
| | | Statistically Significant Impairment (S) Compared with Population Norms | | | | | | | | | | | | | | | | | | | | | |
| SF-36 Subscales | Physical Function | S | S | S | S | | S | S | S | S | S | S | S | S | S | S | S | S | S | | | S | |
| | Role Physical | S | S | S | S | S | S | | S | S | S | S | S | S | S | S | S | S | S | S | | | S |
| | Bodily Pain | S | S | | S | | | S | | S | S | S | S | | | S | S | S | | | | S | |
| | General Health | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S |
| | Vitality | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | | | | |
| | Social Functioning | S | S | S | S | S | S | S | S | S | S | S | S | | S | S | S | S | S | S | S | | S |
| | Role-Emotional | S | S | | S | S | | S | S | | S | S | S | S | S | S | S | S | S | S | | | S |
| Mental Health | | S | S | | S | S | | S | S | | S | S | S | S | S | S | S | S | S | | | | S |

Table 1: Studies comparing HRQoL in individuals with HCV versus healthy controls or population norms, using SF-36 or HQLQ tools.

Foster, Goldin and Thomas (1998) reported a reduced HRQoL in patients with HCV which could not be attributed to either the degree of liver disease, or association with a history of injecting drug use, concluding the decrement was attributable to HCV *per se*. Clearly, whilst only looking at these two parameters there remained the possibility that the differences observed could be due to other, as yet unmeasured factors. Bonkovsky *et al* (1999) sought to address this by observing the effect that successful antiviral treatment had on patients' HRQoL. They hypothesised that if HRQoL improved upon effective removal of the virus, then the virus itself was the true cause of the impairment. They reported data from a large multi-centre drug trial which supported this hypothesis, concluding that HCV infection reduces HRQoL independent of comorbidities or factors associated with the virus (Bonkovsky *et al*, 1999)¹¹. Research from real-world populations has also given weight to the argument that viral factors contribute to HRQoL independent of host-factors (John-Baptiste *et al*, 2009; Strauss, Porto-Ferreira, Almeida-Neto and Teixeira, 2014), and whilst the mechanism for this is still debated, evidence of viral replication within the central nervous system adds weight to the argument (Forton, Karayiannis, Mahmud, Taylor-Robinson and Thomas, 2004).

Despite such persuasive assertions, it is unlikely that any one factor is solely responsible for reduced HRQoL, and a complex multifactorial cause is a more likely explanation. Virus-related factors and associated extra-hepatic manifestations of HCV, combined with host-related factors, psychiatric and medical co-morbidities and the pressure of societal stigma are all likely to be significant contributors (Daltro-Oliveira, Morais-de-Jesus, Pettersen, Paraná and Quarantini, 2013; Häuser, Zimmer, Schiedermaier and Grandt, 2004; Helbling *et al*, 2008; Hsu *et al*, 2012; Lowry *et al*, 2016). These factors will now be examined.

2.3.2.2 Causal investigation: extra-hepatic manifestations of HCV

Extra-hepatic manifestations of HCV encompass any condition or symptom that affects any organ other than the liver. Among the most common complaints of patients with

¹¹ It should be noted, that patients enrolled in clinical trials represent highly selected populations (Van Spall, Toren, Kiss and Fowler, 2007), and it is not clear whether these results are generalizable, particularly as very little demographic data is given. This will be discussed in greater detail in due course.

HCV is cognitive impairment (commonly referred to as 'brain-fog') which occurs independent of the degree of liver disease present (Forton *et al*, 2002; Kramer *et al*, 2002), but can be more marked in patients with cirrhosis due to the effects of hepatic encephalopathy (Córdoba *et al*, 2003). There is some evidence that the aetiology of cognitive impairment contains a biological cause (Forton *et al*, 2002; Forton *et al*, 2004), implying a direct action of HCV on the brain (Kramer *et al*, 2002; Lowry, Coughlin, McCarthy and Crowe, 2010). It has also been demonstrated that cognitive function improves in patients who are successfully treated for HCV infection (Kraus *et al*, 2013; Thein *et al*, 2007) adding weight to the argument for a direct viral effect. To what degree any subsequent impairment in HRQoL derives from this effect is debatable, as negative decrements have been shown even in the absence of significant cognitive abnormalities (Córdoba *et al*, 2003; Kramer *et al*, 2002). However, it is possible the tools used to measure cognitive abnormalities in these studies lacked sufficient sensitivity. A further consideration is the role of comorbid substance use in cognitive impairment for individuals with HCV. Donoghue and Doody (2012) suggest substance using individuals with HCV may experience a 'double-deficit' in cognitive impairment, impinging more profoundly on their HRQoL. The relationship between HCV, cognitive impairment and HRQoL is therefore not straightforward. Indeed, recent research from Ireland reported little evidence of significant cognitive dysfunction in those with mild liver disease, questioning earlier work in this area (Lowry *et al*, 2016).

Fatigue is also a commonly reported extra-hepatic manifestation of HCV, although the pathophysiology remains poorly understood. It has been found to be independently associated with impairment of HRQoL, and unrelated to the severity of liver disease (Fábregas *et al*, 2013; Kramer *et al*, 2005). A further study supported this assertion and concluded that disabling fatigue was the most important factor contributing to lower HRQoL in HCV patients (Kallman *et al*, 2007). Fatigue has also been shown to improve following successful therapy supporting the argument that there is a direct or indirect viral effect causing fatigue-related HRQoL reduction (Bernstein, Kleinman, Barker, Revicki and Green, 2002; Gerber *et al*, 2016; Hassanein *et al*, 2004; Rasenack *et al*, 2003). Interestingly, a study examining biopsychosocial variables in HCV patients found poor social functioning was the most significant predictor of fatigue (Hilsabeck,

Hassanein and Perry, 2005), and fatigue has also been closely linked to the incidence of depression amongst individuals with HCV (Yamini *et al*, 2011). These findings highlight the difficulties that lie in disentangling what can be attributed to viral factors, and what can be attributed elsewhere.

Whether depression is an extra-hepatic manifestation of HCV and/or a separate underlying pre-morbid psychiatric condition due to associated host-related factors is unproven. However, its presence within the HCV population is common and its effect on HRQoL has been shown (Barboza *et al*, 2016; Lowry *et al*, 2016). Gallegos-Orozco *et al* (2003) reported a 59% incidence of depression in HCV patients, and demonstrated lower HRQoL in this cohort compared to non-depressed HCV patients. Of note, none of the patients in this study had any additional comorbidities, history of injecting drug use or alcohol dependence, suggesting these often cited host-factors did not contribute in this instance, and a viral cause may be involved. Dan *et al* (2006) also highlighted the strongly predictive role a history of depression and pre-treatment depressive symptoms play in HRQoL for patients undergoing treatment, a finding supported by separate work conducted with American Veterans (Rowan *et al*, 2005).

2.3.2.3 Causal investigation: host-related factors

The role of illicit drug use in relation to HRQoL decrements is an important consideration, given the high incidence of current or former PWID within this patient population (Hutchinson *et al*, 2006). People who inject drugs experience a lower HRQoL than population norms irrespective of their HCV status (Dalgard, Egeland, Skaug, Vilimas and Steen, 2004; Fischer, Conrad, Clavarino, Kemp and Najman, 2013; Gjeruldsen, Loge, Myrvang and Opjordsmoen, 2006; McDonald *et al*, 2013), and former PWID who have HCV have been shown to have lower HRQoL than individuals who acquired HCV by another route (Foster *et al*, 1998; Hollander, Foster and Weiland, 2006). Untreated HCV patients on methadone maintenance therapy have also been shown to have lower HRQoL when compared to untreated HCV patients without a substance use diagnosis (Batki, Canfield, Smyth and Ploutz-Snyder, 2009).

Of interest, a study by Dalgard *et al* (2004) reported that active PWID who *believed* they were infected with HCV had poorer HRQoL than those who did not or who did not

know their status, irrespective of their actual serostatus. This implies the knowledge (or assumed knowledge) of HCV positive status impacts HRQoL in addition to actually being infected with the virus (the so-called 'labelling effect'¹²). This echoes earlier work from a much smaller sample which found PWID who were unaware of their HCV positive status had better HRQoL than those who were aware of their infection 26 years after being infected (Rodger, Jolley, Thompson, Lanigan and Crofts, 1999). A recent much larger study from Scotland supports these findings. McDonald *et al* (2013) assessed almost 3000 current PWID accessing injecting equipment provision services in Scotland using the EQ-5D questionnaire and anonymised dried bloodspot testing. They reported a reduction in HRQoL between those who were aware of their HCV positive status and those who were not. Additionally, no difference in HRQoL was found between HCV negative PWID and those who were positive but unaware of their infection, supporting other work suggesting the impact of an undiagnosed HCV infection upon groups with already lower HRQoL than population norms places little additional burden, possibly due to the extent of co-morbidities present and overall lower HRQoL anyway (e.g. Schwarzingner *et al*, 2004; Thein *et al*, 2006).

In exploring the reasons for these findings, it becomes evident that the quantitative data available fails to provide sufficient insight. Why does undiagnosed HCV fail to impact on HRQoL for this population when it has been demonstrated to have a detrimental effect in other groups such as blood donors (e.g. Ferreira, de Almeida-Neto, Teixeira and Strauss, 2015; Strauss *et al*, 2014)? Is the negative 'label' of HCV constructed around preconceptions to the chronic nature of the virus and its poor treatment outlook, or from external influences such as societal stigma? These points will be returned to in due course, when the qualitative literature surrounding the lived experience of HCV is examined.

In addition to substance use, other comorbid psychiatric and medical problems have been implicated in reducing HRQoL for individuals with HCV (Hsu *et al*, 2012; Taliani *et al*, 2007). Häuser *et al* (2004) noted that comorbidity is the best predictor of overall

¹² Labelling theory was first described by sociologists in relation to deviance and criminal behaviour, focusing on the tendency of populations to negatively label minorities who deviate from cultural norms. The theory has been modified and expanded in several fields, describing how an individual can incorporate a negative label into their own self-concept.

HRQoL reduction in patients with HCV, describing both psychiatric illness and somatic medical problems as equally relevant. Further studies also highlighted the importance of underlying medical and psychiatric comorbidities in reductions to both the mental health domains (Lim *et al*, 2006; Snow *et al*, 2010) and the physical domains (Kwan *et al*, 2008) of HRQoL.

Various demographic factors have also been demonstrated to have an effect over HRQoL in HCV patients, although the evidence is inconsistent. Female gender has been reported to both affect (Bezemer *et al*, 2012; Bonkovsky *et al*, 2007; Kallman *et al*, 2007; Kuwashiro *et al*, 2014; Miller, Hiller and Shaw, 2001; Taliani *et al*, 2007; Younossi *et al*, 2016e) and not affect (Bonkovsky *et al*, 1999; de Souza, Villar, Garbin, Rovida and Garbin, 2015; Fábregas *et al*, 2013; Helbling *et al*, 2008) HRQoL, and, similarly, age has shown decrements for those less than 40 years old (Miller *et al*, 2001) as well as those in the over 40 year old age bracket (Bezemer *et al*, 2012; El Khoury, Vietri and Prajapati, 2014; Kramer *et al*, 2005). Other factors such as non-married status (e.g. Fábregas *et al*, 2013; Hsu *et al*, 2009; Hsu *et al*, 2012), cigarette smoking (Balfour *et al*, 2006), low household income (Alves *et al*, 2012; de Souza *et al*, 2015; Hsu *et al*, 2009) and lower as well as higher educational level (Alves *et al*, 2012; El-Seoud *et al*, 2008) have also been cited as a reason for poorer HRQoL in HCV patients in studies where this data has been collected. Such findings emphasise the fact that only those sociodemographic factors collected in individual studies can be tested for significance, providing no indication of whether a particular potentially unreported factor may also be causing HRQoL decrements and actually be of greater significance to the patients themselves.

2.3.2.4 Causal investigation: stigma

A final factor to note with respect to HRQoL decrements is that of societal stigma towards individuals with HCV. As already described, PWID who were aware of their infection had lower HRQoL than those who were unaware (Rodger *et al*, 1999; McDonald *et al*, 2013) with the authors noting that this may be due in part to the effects of stigmatisation towards these individuals and also of 'self-labelling' affecting personal psychological health (Rodger *et al*, 1999). In one of the very few studies to combine a qualitative approach with a quantitative HRQoL questionnaire, Miller *et al*

(2001) described patients' distress by the perceived stigma associated with HCV. However, without this qualitative adjunct the effects of stigma may be lost, or only theorised about, in the majority of HRQoL quantitative research. Paterson *et al* (2007) note that infectious diseases (such as HCV), mental illness, and drug and alcohol dependence carry particularly strong societal stigma. Therefore, being unable to account for this specific effect is a major limitation for the majority of PROM questionnaire-based HRQoL research given the population being studied. This point will be returned to when the qualitative literature around this topic is examined.

2.3.3 HRQoL pre-treatment

The impairment in HRQoL for individuals with HCV has been shown to be equivalent to, or more severe than, the impact on physical and general health experienced by individuals with other chronic conditions such as hypertension, type II diabetes, arthritis or depression (Bayliss *et al*, 1998; Bonkovsky *et al*, 1999; Kallman *et al*, 2007). Hepatitis C has greater impact on the physical domains of HRQoL than hepatitis B in mono-infection (Bondini *et al*, 2007; Foster *et al*, 1998) and when studied in HIV co-infected individuals (Gillis *et al*, 2013). Of note, HCV also significantly impacts mental health, an area in which decrements in other conditions are generally smaller (Foster, 2009; Tillmann *et al*, 2011). This reduction in HRQoL can occur even in the absence of cirrhosis or significant liver disease (Bonkovsky *et al*, 1999; Córdoba *et al*, 2003; Foster *et al*, 1998; Häuser *et al*, 2004; Helbling *et al*, 2008; Rowan *et al*, 2005), and does not appear to be associated with Alanine Aminotransferase (ALT) levels¹³ (Arora *et al*, 2006; Foster *et al*, 1998; Helbling *et al*, 2008; Miller *et al*, 2001; von Wagner *et al*, 2006). Where advanced significant liver disease does occur, however, further reductions in HRQoL are reported on a sliding continuum from advanced bridging fibrosis, to compensated cirrhosis to decompensation (Björnsson *et al*, 2009; Bonkovsky *et al*, 2007; Córdoba *et al*, 2003; Kallman *et al*, 2007; Snow *et al*, 2010). Although most HRQoL domains are affected, reductions in the physical components are most frequently noted as being most sensitive to the negative impact of cirrhosis (Bayliss *et al*, 1998; Bonkovsky *et al*, 2007; Córdoba *et al*, 2003; Kallman *et al*, 2007; Mandorfer *et al*, 2014). This low HRQoL in untreated HCV patients has been reported

¹³ ALT is an enzyme mainly found in the liver, although low levels are also normally found within the blood. A rise in ALT levels in the blood can indicate the liver is damaged or diseased.

to have substantial economic costs to society, through loss of productivity, increased absenteeism from work and increased use of healthcare resources (El Khoury, Vietri and Prajapati, 2012; Liu *et al*, 2012).

2.3.4 HRQoL during treatment

2.3.4.1 The early years

The treatment of HCV has long been associated with a further transient reduction in HRQoL, largely attributed to the drugs used during therapy. Individuals treated with interferon, with or without ribavirin, demonstrated a significant increase in depression (Hunt *et al*, 1997), severe treatment-related distress (Bianchi *et al*, 2000) and a general decline in HRQoL during their period of therapy. These then returned to or surpassed baseline levels by 24 weeks post-treatment for those who achieved an SVR (McHutchison *et al*, 2001; Ware, Bayliss, Mannocchia, Davis and the International Hepatitis Interventional Therapy Group, 1999). With the pegylation of interferon, a reduced impairment in HRQoL and less fatigue were reported during pegylated-interferon and ribavirin therapy compared to interferon and ribavirin, especially in the initial 12-24 weeks, which had important implications for reducing treatment discontinuation (Bernstein *et al*, 2002; Hassanein *et al*, 2004; Mathew, Peiffer, Rhoades and McGarrity, 2006; Rasenack *et al*, 2003). Although improved, the pattern of transient reduction in HRQoL during therapy persisted (e.g. Grotzinger *et al*, 2016), and whilst the majority of these findings were from large multi-centre randomised controlled trials (RCTs), a similar pattern of transient decrement in HRQoL has been described in real-world cohorts (Doyle *et al*, 2016; Hollander *et al*, 2006; Kang, Hwang, Lee, Chang and Lee, 2005; Marcellin *et al*, 2011; Matsushita *et al*, 2014; Sinakos *et al*, 2010) and in HIV/HCV co-infection (Kemmer *et al*, 2012; Mandorfer *et al*, 2014; Thein *et al*, 2007).

2.3.4.2 The arrival of the DAAs

The advent of triple therapy for HCV saw the standard of care for HCV genotype 1 evolve, with the addition of DAAs to the existing pegylated-interferon and ribavirin regimen (SIGN, 2013). The first of these drugs to become available were the NS3/4A protease inhibitors telaprevir and boceprevir. Vera-Llonch *et al* (2013) reported data from a phase III, placebo-controlled RCT which assessed the efficacy of various

telaprevir-based regimens in comparison to 48 weeks of pegylated-interferon and ribavirin. They reported a greater transient reduction in HRQoL during the first 12 weeks of therapy in the telaprevir arms of the study, which negatively affected work productivity and may also have had implications for treatment adherence (Aggarwal *et al*, 2015).

This exacerbation of the on-treatment decrement in HRQoL was short-lived, however. As HCV treatment continued its rapid evolution, pangenotypic data from RCTs involving second generation DAAs became available for HRQoL timeously alongside hard biomedical endpoints such as SVR. The RCTs involving the polymerase inhibitor sofosbuvir were the first to report HRQoL data for interferon-*free* regimens. These showed significantly less impairment during therapy, although a modest decrement still remained during the twelve-week treatment duration (Younossi *et al*, 2014a; Younossi *et al*, 2014b). This decrement was attributed mainly to ribavirin and its associated side effects by the authors, and improved upon treatment cessation (Younossi *et al*, 2014b; Younossi *et al*, 2014c; Younossi *et al*, 2016a)¹⁴. Similar improvements in HRQoL with other interferon-free regimens have reported similar findings (Dore *et al*, 2016).

The arrival of interferon- *and* ribavirin-free regimens has, for the first time, seen reports of significant and persistent *improvements* in HRQoL during treatment, rather than a transient decline (Lawitz *et al*, 2016; Younossi, Stepanova, Nader, Lam and Hunt, 2015; Younossi *et al*, 2016a; 2016b; 2016c; Younossi, Stepanova, Nader and Henry, 2016d). Such improvements have been described as early as four weeks into therapy, and linked to viral eradication rather than simply the ‘excitement’ of receiving these new, highly efficacious treatments (Younossi *et al*, 2016c). Improvements in

¹⁴ The role of ribavirin in HCV treatment bears brief, closer inspection, as it has often been overlooked due to the comparative severity of interferon-related side effects. In early studies comparing pegylated-interferon monotherapy with (pegylated-) interferon and ribavirin dual therapy regimes, the observed impairments in HRQoL during therapy were substantially exacerbated by ribavirin (Hassanein *et al*, 2004; Perrillo *et al*, 2004). A possible mechanism for this is ribavirin-associated haemolytic anaemia, which is an important factor in determining HRQoL during anti-viral therapy, impacting physical functioning, work-related activities and fatigue (Dan *et al*, 2006; Falasca *et al*, 2009; Hollander *et al*, 2006; Mandorfer *et al*, 2014). Perhaps surprisingly therefore, Younossi *et al* (2014b) report that in patients receiving sofosbuvir and ribavirin, a more profound and clinically significant decrement is seen in the mental health aspects of HRQoL compared to the physical parameters. They hypothesised that previously suspected neuropsychiatric side effects of ribavirin may be involved.

HRQoL during interferon- and ribavirin-free treatment have been shown in both HCV mono-infected and HIV/HCV co-infected individuals (Younossi *et al*, 2016e; 2016f). In addition, specific work focused on Asian cohorts has reported similar findings (Ikeda *et al*, 2016; Younossi *et al*, 2016a; 2016g; 2016h). However, as this data is exclusively from RCTs it remains to be seen whether a similar scenario is observed in more representative patient populations.

2.3.5 HRQoL post-treatment

For patients who persist with therapy and achieve an SVR, benefits of treatment have been reflected in improvements to both physical and mental health domains of their HRQoL compared to non-responders, and in relation to their own baseline scores (table 2). This applies in patients with persistently normal ALT (Arora *et al*, 2006; Bini and Mehandru, 2006) as well as those with advanced fibrosis and cirrhosis (Bernstein *et al*, 2002; Bonkovsky *et al*, 2007; Younossi *et al*, 2014a). Individuals who are co-infected with HIV/HCV who achieve SVR have also similarly shown improvements in physical and general health, fatigue, and cognitive function (Kemmer *et al*, 2012; Mandorfer *et al*, 2014). Studies in non-Western populations confirm similar findings (Kang *et al*, 2005).

| Author and Year | | Ware <i>et al</i> (1999) | Bonkovsky <i>et al</i> (1999) | McHutchison <i>et al</i> (2001) | Bernstein <i>et al</i> (2002) | Rasnick <i>et al</i> (2003) | Hassanein <i>et al</i> (2004) | Kang <i>et al</i> (2005) | Mathew <i>et al</i> (2006) | Hollander <i>et al</i> (2006) | Bini & Mehandru (2006) (Results for normal ALT group) | Bini & Mehandru (2006) (Results for elevated ALT group) | Arora <i>et al</i> (2006) | Bonkovsky <i>et al</i> (2007) | Thien <i>et al</i> (2007) | Marcellin <i>et al</i> (2011) | Beziere <i>et al</i> (2012) | Isaacs <i>et al</i> (2013) | Younossi <i>et al</i> (2014a) * | Younossi <i>et al</i> (2014c) * | Younossi <i>et al</i> (2014b) * | Younossi <i>et al</i> (2016c) * | | |
|----------------------|--------------------------------|--|-------------------------------|---------------------------------|-------------------------------|-----------------------------|-------------------------------|--------------------------|----------------------------|-------------------------------|--|--|---------------------------|-------------------------------|---------------------------|-------------------------------|-----------------------------|----------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|-----|-----|
| n = | | 324 | 704 | 912 | 1441 | 531 | 1121 | 371 | 152 | 147 | 46 | 92 | 491 | 1144 | 34 | 1860 | 128 | 118 | 192 | 334 | 215 | 201 | 327 | 624 |
| Clinical Trial Data? | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | | | ✓ | ✓ | | | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| | | Significant (S) Improvement or Trend Towards (T) at SVR Compared to Baseline Reading | | | | | | | | | | | | | | | | | | | | | | |
| SF-36 Subscales | Physical Function | | S | S | S | S | S | S | | | S | S | | | S | | | | | | | S | | S |
| | Role Physical | | S | S | S | S | S | S | | S | S | S | | S | S | | | S | | | | T | | S |
| | Bodily Pain | | | S | S | S | S | S | | | S | S | | | | | | | | S | S | | | S |
| | General Health | S | S | S | S | S | S | S | | S | S | S | S | S | S | | | S | | S | S | | S | S |
| | Vitality | S | S | S | S | S | S | S | T | S | T | S | S | S | S | | | | S | S | | S | S | S |
| | Social Functioning | S | S | S | S | S | S | S | S | T | S | T | S | | | S | | S | S | | | | | S |
| | Role-Emotional | | | | S | | S | S | T | | S | S | | S | S | | | | S | | | | | S |
| | Mental Health | | | | S | S | S | S | | | S | | | | | S | | | | | | | S | S |
| | Physical Component Score (PCS) | | | | S | S | S | | | | S | S | S | | S | S | | | | S | T | S | | S |
| Additional Scales | Mental Component Score (MCS) | | | | S | S | S | | | | S | | | S | S | | | | | | | | | S |
| | Sleep | | | | | | | | | | S | T | | | | | | | | | | | | |
| | Health-Distress | S | | | | | | | | | | S | | | | | | | | | | | | |
| | CHC Health-Distress | S | | | | | | | | | T | | | | | | | | S | | | | | |
| | CHC Limitations | S | | | | | | | | | S | | | | | | | | S | | | | | |

Table 2: Studies comparing HRQoL in individuals with HCV who achieve SVR compared to their baseline levels, using the SF-36 or HQLQ tools (*indicates SVR12 reported)

The HRQoL domains in which improvements are reported following SVR are not consistent however (table 2), and indeed in some studies have not been found at all (Tillmann *et al*, 2011). A number of studies found improvement only in physical domains compared to baseline readings (Bonkovsky *et al*, 1999; Hollander *et al*, 2006; Isaacs, Abdelaziz, Keller, Tibble and Haq, 2013; McHutchison *et al*, 2001; Ware *et al*, 1999) with others reporting only physical and not emotional increments when patients who achieve SVR are compared with those who remain viraemic (Helbling *et al*, 2008). Another study also showed less improvement in mental health scores compared to physical and sexual health leading the authors to argue that HCV *per se* has minimal effect on emotional states (Bonkovsky *et al*, 2007). Conversely, a study of co-infected HIV/HCV patients found some benefit to mental health (but not physical health) for patients who *did not* achieve an SVR, theorising that a reduction in HCV viral load during treatment may provide some benefit to patients (Thein *et al*, 2007). With the major differences between results from the reported studies, it is important to examine the various limitations that may have influenced these findings.

2.3.5.1 Limitations and weaknesses

The time-point at which post-treatment HRQoL is measured could potentially influence the results obtained. For example, Pojoga, Dumitraşcu, Pascu and Grigorescu (2006) concluded that antiviral therapy does not improve HRQoL, but took their post-treatment measurement immediately after interferon and ribavirin therapy had finished. In contrast, John-Baptiste *et al* (2009) took a cross-sectional approach and reported that patients who had achieved an SVR had improved HRQoL, higher employment and better productivity at work, leisure and around the house at an average of 3.7 years post-therapy (although due to its cross-sectional nature, this result is limited by the retrospective recollection of respondents). The majority of studies have measured for improvement in HRQoL alongside the hard medical endpoint at 24 weeks post end of treatment. However, this is generally for the convenience of data collection and from a HRQoL viewpoint is an arbitrary time-point. Helbling *et al* (2008) also note that at this point the positive emotional response due to treatment success is still strong, possibly influencing responses. More recently, measurement of SVR at week 12 post-treatment has been accepted as a primary end point for most clinical trials (Chen *et al*, 2013) meaning the published trials using DAAs

are reporting HRQoL data from patients at SVR12 and not SVR24 (e.g. Dore *et al*, 2016; Younossi *et al*, 2014a; Younossi *et al*, 2014b; Younossi *et al*, 2016a; Younossi *et al*, 2016b), possibly when the emotional response is even stronger, or the effects of treatment are still being felt.

Another frequently reported limitation in the literature is that of patient awareness of their serological result prior to completion of the study PROM tools. In the same way that knowledge of being HCV positive influences HRQoL (Häuser *et al*, 2004, McDonald *et al*, 2013; Rodger *et al*, 1999), do patients *feel* better, simply because they know they have now cleared the infection? McHutchison *et al* (2001) argued that as changes in HRQoL are seen in different SF-36 domains and not reported 'across-the-board', it was unlikely that awareness of SVR was entirely responsible for the observed improvements. A later study which blinded serological results to patients and investigators found improvements in mental health for patients who had undetectable HCV RNA at week 12 of therapy compared to those who remained detectable (Quarantini *et al*, 2008), supporting the theory that knowledge of infection cannot account for all HRQoL increases alone.

2.3.6 A different paradigm

The quantitative literature deals primarily with HRQoL cause and effect, reducing the burden of illness to numeric estimates which may demonstrate statistical and clinical significance, but the patient experience, and the patient voice, remains silent.

However, as previously stated, PROMs is an umbrella term incorporating any report coming directly from a patient about their health condition and treatment. With this in mind, there is also a body of qualitative research providing more in-depth exploration of the lived experience of HCV. This qualitative approach can be used to add 'flesh-to-the-bones' of what has been reported within the quantitative literature. For example, Hopwood and Treloar (2005) explored the reported on-treatment decrement in HRQoL by using patients' narratives to gain an insight into their experience of side-effects, and how coping with these impacted on their daily lives. However, qualitative data can do more, as demonstrated by Miller *et al* (2001) in their mixed methods study. It can illuminate impairments not captured by HRQoL instruments such as the role of stigma, and explore social and psychological factors

impacting on HRQoL and day-to-day living that are beyond what is measureable by psychometric questionnaires such as the SF-36. In doing so, a more detailed and vivid picture of the impact of HCV can be built. With this in mind, we turn to the qualitative literature focused on the lived experience of HCV, and examine the main themes present in that body of work, beginning with the experience of diagnosis.

2.3.7 Diagnosis

A number of studies have drawn on the theory of chronic illness as biographical disruption (Bury, 1982) to provide insight into their participants' narratives of HCV diagnosis¹⁵. For many, an initial reaction of shock was accompanied by overwhelming feelings of fear, denial, anger and depression (Glacken, Kernohan and Coates, 2001; Groessl *et al*, 2008; Janke, McGraw, Garcia-Tsao and Fraenkel, 2008; Olsen, Banwell and Dance, 2012; Sgorbini, O'Brien and Jackson, 2009; Sutton and Treloar, 2007; Tompkins, Wright and Jones, 2005). Faye and Irurita (2003) describe their participants feeling condemned, with their futures being forfeited:

It was a death sentence. Not knowing a lot about it, and asking my doctor if I was going to die in ten years and he couldn't tell me.

(Faye and Irurita, 2003, p.94)

This 'fear of the unknown' was an emerging theme from a number of studies around this time (Carrier, LaPlante and Bruneau, 2005; Groessl *et al*, 2008). However, due to how rapidly HCV knowledge has grown over the last decade, it should be viewed within the context of when the research was undertaken. That said, a more recent article by Hill *et al* (2015) suggests that the sustained uncertainties of life with HCV results in individuals feeling their futures are uncontrollably dictated by the virus.

For participants who had a history of injecting drug use, reactions to HCV diagnosis were sometimes modified and tempered, either because they suspected they were

¹⁵ Medically, HCV is defined as a chronic infection if it does not spontaneously resolve within the first six months following acquisition (Seeff, 2002). Chronicity within the context of theoretical models, and this literature review, is taken to mean an individual's perception that their condition will be one which is long-term. The social construction of chronic illness literature gives phenomenological perspectives on personal naturalistic accounts of 'lived illness', which provides a basis for this understanding (Martin and Peterson, 2009).

HCV positive anyway (Olsen *et al*, 2012; Temple-Smith, Gifford and Stoové, 2004), or because of multiple HCV diagnoses within their peer group around the same time. These provided context and mitigated the impact (Fry and Bates, 2012). It also served as an unwelcome reminder of a previous time in their lives, potentially exposing an earlier identity that many had worked hard to put behind them (Fry and Bates, 2012; Grundy and Beeching, 2004; Hill *et al*, 2015; Olsen *et al*, 2012):

I was thrown right back there and it was awfully upsetting because I really did think that that time of my life was past and that I'd come to terms with grief and difficulty and all sorts of things in my life. And what happened? The legacy...

(Fry and Bates, 2012 p.467)

For individuals who had been experiencing significant symptoms of HCV such as unexplained fatigue, the intensely negative reaction to their HCV diagnosis also came with a sense of relief as their health problems had finally been formally identified and medically labelled (Copeland, 2004; Glacken *et al*, 2001; Groessl *et al*, 2008). Interestingly, the reaction of current PWID to a HCV diagnosis appears to be significantly less traumatic, not conforming to Bury's (1982) concept and perhaps representing more 'biographical reinforcement' (Carricaburu and Pierret, 1995) than 'biographical disruption'. This issue will be discussed in greater detail in due course.

Following diagnosis, the re-evaluation of an individual's life and an attempt to regain control are commonly reported. Glacken *et al* (2001) describe diagnosis as a catalyst for the re-examination of life priorities, often resulting in making more time for partners and children. Faye and Irurita (2003) describe this process as 'balancing perspective', integrating HCV into a comfortable, acceptable and balanced future life. For many, instigating positive health behaviours which served to exert control over HCV was important, including changes to dietary habits, exercise regimes and drinking patterns (Fry and Bates, 2012, Glacken *et al*, 2001; Hill *et al*, 2015; Paterson *et al*, 2006; Roy, Nonn, Haley and Cox, 2007; Sutton and Treloar, 2007). However, by making these changes, life could feel restricted and no longer normal (Conrad, Garrett, Cooksley, Dunne and MacDonald, 2006; Hill *et al*, 2015). A lack of information and understanding of HCV at diagnosis could also hinder this process, denying the sought

after sense of control and exacerbating prognostic uncertainty (Glacken *et al*, 2001; Sutton and Treloar, 2007). Many people actively sought out information in order to expand their knowledge on the nature of the condition post-diagnosis (Fry and Bates, 2012; Glacken *et al*, 2001; Groessl *et al*, 2008; Jiwani, Begum Gal, Ali, Salih and Hanzala, 2013; Roy *et al*, 2007; Tompkins *et al*, 2005) helping them to engage in their re-evaluation of life. This process also encompassed a passage of time, which has been described as another key dimension moderating the accommodation of HCV into future life plans (Treloar and Rhodes, 2009).

This literature provides insight into the way HCV is viewed as a chronic condition following diagnosis, and how individuals seek ways in which they are able to live with the disease. However, the delivery of healthcare is dominated by an acute care model focused on treatment and cure which can create frustration due to competing agendas (Paterson *et al*, 2006). The self-management strategies outlined above can be catalysed by the narrow focus of the medical model experienced from healthcare professionals (Fry and Bates, 2012), with psychosocial aspects of the disease often remaining unaddressed by providers (Hill *et al*, 2015; Paterson *et al*, 2006; Sheppard and Hubbert, 2006). A further problem arises from the adoption of an acute medical model for patients who achieve SVR yet remain symptomatic post-treatment and continue to view themselves as chronically ill. Hepatitis C providers consider them cured and will no longer care for them (Hopwood, 2013; Paterson *et al*, 2006). The exploration of reaction to a HCV diagnosis, and subsequent theoretical modelling of chronic illness has to date been conducted within the era of pegylated-interferon monotherapy, or pegylated-interferon and ribavirin dual therapy. With the treatment landscape rapidly evolving, and drug efficacy and tolerability making astounding improvements in recent years, it is unclear whether chronic illness models remain relevant to a disease that is becoming increasingly curable for those who access treatment.

2.3.8 The lived experience of HCV

2.3.8.1 Fatigue

Fatigue is one of the most commonly reported symptoms of HCV (Conrad *et al*, 2006; Fry and Bates, 2012; Glacken *et al*, 2001; Glacken, Coates, Kernohan and Hegarty,

2003; Groessl *et al*, 2008; Jiwani *et al*, 2013; Zalai, Carney, Sherman, Shapiro and McShane, 2016), and a greater understanding of how this impacts HRQoL starts to emerge when reviewing the qualitative data. Sutton and Treloar (2007) describe individuals losing their strength and energy, affecting performance at work, in sport and socially. The need to prioritise what energy they have in both the short- and long-term also appears important. Short-term strategies include withdrawing from social activities, and reducing their share of parenting and domestic duties. Long-term approaches may include deciding to have fewer children or altering broader life plans (Fry and Bates, 2012). Unsurprisingly, such prioritisation can lead to relationship stress and personal feelings of uselessness, which will further impact on HRQoL and add additional dimensions to the experience of HCV fatigue (Fry and Bates, 2012; Zalai *et al*, 2016). The fatigue experienced has been described as discernible from 'normal fatigue' and multidimensional in nature, perniciously impacting on physical, cognitive and affective dimensions, creating a whole body feeling of fatigue that cannot be relieved by rest (Glacken *et al*, 2001; Glacken *et al*, 2003):

You cannot fight it; it is not a tiredness that you can fight like a normal tiredness. A normal tiredness, you can fight it and get a second wind or if you had a few cups of coffee, it would keep you going. None of this works with this tiredness

(Glacken *et al*, 2003 p.247)

The unpredictability of symptoms has also proved challenging. A number of studies describe sporadic and episodic experiences of HCV illness (Conrad *et al*, 2006; Sutton and Treloar, 2007) which have a high impact on life when they occur, but, when absent, serve to reinforce a notion that the virus is not currently affecting health (Swan *et al*, 2010). This fluctuating and almost arbitrary nature of symptoms makes forward-planning difficult, creating significant uncertainty (Hill *et al*, 2015).

2.3.8.2 Onward transmission

The possibility of inflicting the virus on others has evoked strong reactions in a number of studies, with some participants citing it as a far greater HRQoL issue than any physical symptoms experienced (Conrad *et al*, 2006). Fears around accidentally transmitting HCV have been described, with individuals taking overly cautious

household precautions (Grundy and Beeching, 2004) or displaying more extreme behaviour changes such as a fear of leaving the house in case they become involved in an accident (Fraser and Treloar, 2006). Women have discussed worries over vertical transmission to children (Conrad *et al*, 2006; Temple-Smith *et al*, 2004), which in addition to causing possible disruption to plans for a family, can also impact sex lives and relationships (Grundy and Beeching, 2004; Jiwani *et al*, 2013). The knowledge that HCV is contagious, and subsequent fear of transmission to others, forms a large part of the psychological impact of living with HCV, eliciting constant feelings of anxiety and sadness (Hill *et al*, 2015). Further, expectations of finding a partner and eventually having children are re-evaluated in light of a diagnosis with a contagious disease (Faye and Irurita, 2003; Sutton and Treloar, 2007; Tompkins *et al*, 2005).

2.3.8.3 Impact on PWID

As previously mentioned, the reaction of active PWID to a HCV diagnosis appears significantly less traumatic than those who stopped injecting many years ago and those who acquired HCV through another route. A lack of shock following the diagnosis is described in a number of studies (Faye and Irurita, 2003; Groessl *et al*, 2008; Harris, 2009) accompanied by a sense of inevitability due to its prevalence within their social networks (Hill *et al*, 2015; Olsen *et al*, 2012; Sutton and Treloar, 2007). A commonly reported consequence of HCV diagnosis is an intense and overwhelming depression. However, in PWID this has been described as shallow, and nothing to be dwelt on (Faye and Irurita, 2003) epitomised by a “*what’s done is done, I can’t change it now...*” attitude (Tompkins *et al*, 2005, p.265). Davis and Rhodes (2004) note that HCV is constructed as something acquired rather than caught among the sample of PWID they interviewed in London, language that implies transmission is unavoidable, normalized and almost acquired over time. They remark that due to messages about how transmissible HCV is in comparison to HIV, individuals were left with the understanding that HCV was everywhere and therefore a ubiquitous risk (Davis and Rhodes, 2004). Wozniak, Prakash, Taylor and Wild (2007) explored in more detail this normalization of HCV amongst PWID in Canada, describing social accommodation of the infection, and HCV as a defining characteristic of injecting drug use. Further work from Australia reiterates these perceptions, with one study participant articulating her experience:

And nobody talked about hep C really. I mean you know, in passing, it was just so assumed everybody had it. And nobody saw it as a big deal. No-one was thinking about it. Nobody thought it was anything other than just a complete minor detail that had no bearing on life at all.

(Harris, 2009 p.1032)

Hepatitis C is therefore viewed as part of the identity of being a person who injects drugs by individuals within that social network (Olsen *et al*, 2012; Roy *et al*, 2007). This resonates with studies focused on other conditions; for example, how HIV has become more normalized and socially accommodated amongst gay men (Deacon, Mooney-Somers, Treloar and Maher, 2013). Roy *et al* (2007) suggest that an HCV diagnosis could actually have a positive significance for some, as it enables the individual to feel just like everyone else in their situation, or “... one of the gang, like” (Roy *et al*, 2007 p.400). These ambivalent views towards disease diagnosis are at odds with Bury’s (1982) account of biographical disruption, and instead appear to reinforce conceptions of self-identity and personal biography (Carricaburu and Pierret, 1995) adopting a discourse of normalization (Davis and Rhodes, 2004; Harris, 2009; Wozniak *et al*, 2007). HCV infection is synonymous with injecting drug use, and therefore injecting drug use will naturally lead to HCV infection (Olsen *et al*, 2012). Even without normalization or social accommodation of the disease amongst PWID, Harris (2009) discusses the contextual nature of biographical disruption, and notes that HCV may still have limited impact on life as the diagnosis is often lost in a sea of multiple disruptions. Copeland (2004) describes a similar experience from her work with PWID in Edinburgh, with apathy towards having HCV perhaps stemming from multiple traumas faced in day-to-day lives, and the significance of being HCV positive eclipsed by their problematic existences and identity as a ‘problem drug user’. For those with an uncontrolled drug addiction, life can be spent finding money to feed the habit, crowding out other non-drug related concerns so it “just consumes every part of you” (Swan *et al*, 2010 p.759). If the severity of HCV in relation to other more immediate life-threatening conditions (such as overdose) is considered, health problems that may not develop for many years such as those linked to HCV are unlikely to be overly concerning or prioritised (Roy *et al*, 2007). In their study of Australian women with HCV, Olsen *et al* (2012) note that those currently injecting had fewer social and

economic resources (were more likely to be unemployed, poorly educated, and reliant on housing and financial benefits) which reflected in their HCV discourse:

Within this lifestyle I tend to forget I've got it [HCV] most of the time...when people ask me what's wrong with me I sort of reel off the list and that's the last thing – 'oh that's right, I've got hep C'

(Olsen *et al*, 2012 p.535)

Many PWID are familiar with material hardship, pain, suffering and the possibility of death long before they receive an HCV diagnosis, accounting for how little disruption that diagnosis often brings to their lives (Harris, 2009). Williams (2000) astutely notes that biographical disruption is perhaps more keenly felt among the privileged rather than disadvantaged sections of society. In addition to having little immediate impact, the nature of an injecting drug-use lifestyle means PWID often do not hold long-term future life perspectives, instead focusing on more immediate day-to-day problems (Faye and Irurita, 2003). Copeland (2004) suggests that low self-esteem and a sense of worthlessness forged from traumatic childhood experiences, and an underlying sense of hopelessness amongst PWID contribute to an inability to look to the future. Activities that therefore seek to improve an unimaginable future, such as HCV treatment, are not options worth considering or investing in (Roy *et al*, 2007).

As well as being contextualised within an individual's life, a diagnosis of HCV is often described in relation to HIV/AIDS (Copeland, 2004; Cullen, Kelly, Stanley, Langton and Bury, 2005; Davis and Rhodes, 2004; Harris, 2009; Roy *et al*, 2007; Swan *et al*, 2010; Tompkins *et al*, 2005; Wozniak *et al*, 2007). HIV is often defined as the primary viral risk for injecting drug use, with the seriousness of HCV being undermined by HIV (Davis and Rhodes, 2004). Comments from a couple of studies demonstrating participants' reactions at diagnosis serve to highlight this point well:

I wouldn't mind but I was in bits waiting for the results...the doctor was there going 'now...you have hepatitis C.' I was there going 'hurry up and tell me about the [HIV] virus'

(Cullen *et al*, 2005 p.74)

She told me 'everything looks fine, except it's written positive next to hepatitis C'. So I said to her, 'can I see? I hope I don't have AIDS'

(Roy *et al*, 2007 p.400)

Even in HIV/HCV co-infection, a diagnosis of HCV can be over-shadowed by already having HIV (Copeland, 2004). As public health strategies such as needle exchanges were initially introduced to combat HIV transmission (Robertson and Richardson, 2007), the focus on initial harm-reduction messages for people who use drugs centred on HIV prevention, with HCV appearing within this framework later as an additional concern (Davis and Rhodes, 2004; Harris, 2009). This 'lesser of two evils' perception appears to pervade, with HCV presented as relatively benign in comparison to HIV, and cited as a reason why further investigations and treatment are not accessed post-diagnosis (Swan *et al*, 2010).

The fact that HCV is often asymptomatic can also contribute to its low priority status in lives with many competing demands. Although fatigue, cognitive impairment and depression have all been previously described, these are not ubiquitous. Where they do occur, they may not always be attributed to HCV by the individual, particularly where there is co-morbid active substance use. Due to the lack of physical impact there is no sense of threat from harbouring the virus (Fraenkel, McGraw, Wongcharatrawee and Garcia-Tsao, 2005) and it can therefore become an insignificant part of people's lives (Sutton and Treloar, 2007). Witnessing PWID 'living normally' and showing no signs of sickness can reinforce the normalisation and social accommodation of HCV within social networks, psychologically and socially preparing other members for a potential diagnosis (Carrier *et al*, 2005; Faye and Irurita, 2003).

Reviewing these narratives as a whole, it could be easy to construe that all PWID are disinterested in their health. However, despite repeated reports of a HCV diagnosis having little impact upon lives (Faye and Irurita, 2003; Olsen *et al*, 2012; Sutton and Treloar, 2007), there are incidences of individuals reacting badly to the news (Sutton and Treloar, 2007; Tompkins *et al*, 2005). For some, an overwhelming sense of contamination has been described accompanied by a response characterized by despair (Fraser and Treloar, 2006). Rather than focusing the individual to address the cause, however, (by potentially seeking treatment), a number of accounts relate a sense that the infection is now with them for life, and, as such, interest in their health may actually decrease:

Oh what's the use? You've got it, it's not going to go away, what's the use?

(Fraser and Treloar, 2006 p.106)

*"What's the point? I'm either going to die from drugs or from liver disease"*¹⁶

(Groessl *et al*, 2008 p.1961)

It is often only when individuals move away from substance use and disengage from those social networks that help is sought for HCV. Harris (2009) describes one participant moving away from the drug using community and starting a relationship with a non-drug using man, and only at that point being exposed to what HCV means in the 'mainstream world'. Similarly, Roy *et al* (2007) note that disengagement from substance use and starting to integrate into mainstream society aids an understanding of the health significance of HCV that was previously absent. People who inject drugs going through an intense period of consumption are less concerned about HCV (Roy *et al*, 2007), and becoming clean and sober appears to facilitate engagement with HCV services (Groessl *et al*, 2008).

2.3.8.4 Stigma

The preponderance of accounts detailing individuals' experience of stigma in relation to HCV create an overriding and pervasive theme within the qualitative literature, and again highlight its relative absence from the quantitative paradigm. The stigma experienced is multifaceted, incorporating a number of factors including the involvement of an infectious agent (Conrad *et al*, 2006; Faye and Irurita, 2003; Fraser and Treloar, 2006) and an association with HIV/AIDS (Zickmund, Ho, Masuda, Ippolito and LaBrecque, 2003). However, the most frequently described association is with illicit injecting drug use (Butt *et al*, 2008; Conrad *et al*, 2006; Faye and Irurita, 2003; Paterson *et al*, 2006; Zickmund *et al*, 2003) propagating the belief that the disease has been acquired through the fault of the sufferer (Fraser and Treloar, 2006). This link to drug use is persistent and tenacious, and stigma and discrimination related to drug use have been experienced by many individuals with HCV irrespective of their mode of

¹⁶ The authors note that immediately after diagnosis, this participant began using drugs again.

acquisition (Butt *et al*, 2008; Faye and Irurita, 2003; Fry and Bates, 2012; Hill *et al*, 2015). This is neatly summed up by a quote from a study which included participants who contracted HCV from a variety of different sources, but excluded PWID:

We are all tarred with the same brush. People think 'hepatitis', yeah they're all drug addicts, and they think 'they've done something wrong'

(Hill *et al*, 2015 p.5)

The wish to avoid this association can lead to disclosure of HCV positive status being followed up with an account of how it was acquired through blood transfusion, irrespective of how the virus was actually caught (Conrad *et al*, 2006). Women have been described as more likely to experience stigma than men (Swan *et al*, 2010; Zickmund *et al*, 2003), although insights from Temple-Smith *et al* (2004) suggest that women may just be more affected by it, rather than experiencing a greater frequency of exposure. They describe HCV positive men as harbouring expectations to be treated poorly because of their serostatus, which justifies stigmatizing behaviour from others when it is encountered and lessens the impact (Temple-Smith *et al*, 2004). Interestingly, there are also reports of individuals experiencing the stigmatising consequences of having a contagious disease associated with drug use, even after they have cleared the virus (Carrier *et al*, 2005).

These stigmatising attitudes are found amongst family, friends and colleagues (Butt *et al*, 2008; Janke *et al*, 2008; Jiwani *et al*, 2013; Zickmund *et al*, 2003). However, within the healthcare setting and during interactions with healthcare professionals, these stigmatising attitudes and behaviours are also frequently encountered (Butt *et al*, 2008; Fry and Bates, 2012; Grundy and Beeching, 2004; Hill *et al*, 2015; Janke *et al*, 2008; Jiwani *et al*, 2013; Miller *et al*, 2001; Sgorbini *et al*, 2009; Temple-Smith *et al*, 2004; Tompkins *et al*, 2005; Zickmund *et al*, 2003). In wider society, stigma towards HCV has also been reported from communities that attract discriminatory societal attitudes themselves, such as the LGBT community (Deacon *et al*, 2013). Whilst a diagnosis of HIV for a gay man may become part of his gay identity and be accepted within that community, HCV is viewed as a 'straight disease' associated with injecting

drug use and therefore a gay man with HCV becomes a 'junkie' and risks losing his previous identity and place within that group (Deacon *et al*, 2013).

The narratives found within this body of work also demonstrate an internalised stigma, where HCV positive individuals assimilate these widely held societal views. For example, multiple references are made to people feeling contaminated, dirty or 'like a leper' (Fraser and Treloar, 2006; Glacken *et al*, 2001; Grundy and Beeching, 2004; Hill *et al*, 2015; Miller *et al*, 2001; Sutton and Treloar, 2007; Zickmund *et al*, 2003), demonstrating a self-image that has been significantly affected by the diagnosis (Butt *et al*, 2008). This also highlights that even where their diagnosis is not explicitly known to others, internalised stigma can be an ever-present and disruptive influence on people's lives, eliciting fear over the possibility they may be exposed, and also guilt because of their perceived dishonesty in non-disclosure (Fraser and Treloar, 2006).

The decision not to disclose a HCV positive status is often borne out of fears around subsequent stigmatisation (Butt *et al*, 2008; Conrad *et al*, 2006; Faye and Irurita, 2003; Fraser and Treloar, 2006; Glacken *et al*, 2001; Hill *et al*, 2015; Jiwani *et al*, 2013; Sgorbini *et al*, 2009; Sutton and Treloar, 2007; Tompkins *et al*, 2005). However, non-disclosure also appears to carry significant personal cost and has a substantial impact on people's lives. By not identifying as HCV positive, the opportunity to obtain support from peers, colleagues and HCV-focused organisations is lost (Faye and Irurita, 2003; Hill *et al*, 2015). In addition, any causal explanation for symptoms being experienced is removed, meaning individuals may have to continue working whilst extremely fatigued, or deny any emotional stress they may be suffering (Butt *et al*, 2008; Fry and Bates, 2012):

It requires a constant vigilance on my part not to let it slip...you always have to appear 'normal' regardless of how you are really feeling

(Glacken *et al*, 2001 p.110)

Non-disclosure can also have more wide-reaching implications. Butt *et al* (2008) describe how one participant in their study quit his job and withdrew socially to conceal the diagnosis and associated symptoms. This voluntary social withdrawal may

seem an extreme reaction. However, it serves to illustrate the impact of deep-seated and entrenched discrimination and stigmatization towards HCV which pervades unchanged throughout the historic literature up to the present day. The case described is also not unique. Janke *et al* (2008) offer further reasons for individuals voluntarily socially isolating themselves besides concerns over stigma, including emotional volatility and symptom management, as well as a loss of desire to seek out social contact and feeling confused and overwhelmed. These findings are echoed in other studies (Blasiolo, Shinkunas, LaBrecque, Arnold and Zickmund, 2006; Tompkins *et al*, 2005).

Clearly, social isolation is not purely a voluntary undertaking however. Glacken *et al* (2001) describe the diagnosis of HCV resulting in participants feeling their 'social identity' had been stripped away, preventing them from maintaining their previous social relationships. Altered behaviour from others due to stigma can also impact on social networks. Fears of contagion and the potential for viral transmission can lead to isolation from loved ones (Blasiolo *et al*, 2006; Groessl *et al*, 2008; North, Devereaux, Pollio, Hong and Jain, 2014; Zickmund *et al*, 2003), in addition to ignorance surrounding the disease leading to frank discrimination from poorly informed family and peers:

Well, it has affected my family, like even my parents and stuff. My mother's afraid to kiss me; she thinks it's like AIDS, you know. It caused a divorce.

(Blasiolo *et al*, 2006 p.4668)

I lost probably half my friends as they don't know what the disease is. They just automatically put up a front. I don't see them anymore – fear of what may happen. So ignorance is how I like to put it.

(Blasiolo *et al*, 2006 p.4668)

2.3.9 The experience of HCV treatment

2.3.9.1 Barriers and facilitators

In addition to offering valuable insights into how HCV impacts on day-to-day life, qualitative research also provides understandings into the experience of HCV treatment, and explores the decision to pursue a course of therapy. Anxiety regarding

interferon-based treatment, poor treatment efficacy, the often asymptomatic nature of the disease, and fear derived from pervasive side-effect ‘horror stories’ are frequently reported as reasons for delaying therapy (Fraenkel *et al*, 2005; Groessl *et al*, 2008; Hill *et al*, 2015; Kinder, 2009; North *et al*, 2014; Swan *et al*, 2010). In addition, social factors such as family commitments and the ability to work are also cited as particularly pertinent considerations (Fraenkel *et al*, 2005; Swan *et al*, 2010; Treloar, Rance, Dore, Grebely and the ETHOS Study Group, 2014).

Fraenkel *et al* (2005) note that for some, trade-offs such as the risk of side-effects and the low chance of a cure do not enter their decision-making process, and treatment is seen as a certainty for them rather than an option, offering a chance to exert control over the infection (Taylor-Young and Hildebrandt, 2009). Seeing others from within their social network come successfully through treatment, or conversely where HCV has contributed to serious illness or death in others, have also both been described as motivators to engage with care (Swan *et al*, 2010). For those who access treatment and undergo a period of interferon-based therapy, a transient decrement in their HRQoL as measured by PROM questionnaires has previously been described. How this decrement is experienced, and how it impacts on daily life is further explored and given greater depth of understanding by the qualitative literature on the topic.

2.3.9.2 Side-effects

In addition to the effects of HCV-related fatigue previously described, those individuals undergoing treatment have also reported significant fatigue as a result of pegylated-interferon and ribavirin drug therapy. Again, the fatigue experienced appears discernible from what would be considered ‘normal fatigue’, with participants often illustrating how their own experience was different from a ‘typical patient’ and also how it differed from any pre-treatment discussion they had had (Sheppard and Hubert, 2006). Participant quotes demonstrate its intensity and persistence:

There were times when I could just have stayed 4 or 5 days in bed, and I mean 23 out of 24 hours of just laying down

(Zickmund *et al*, 2006 p.383)

Sometimes...I'm flat out making it to where I want to sit down because I actually can feel myself shutting down...just all of a sudden, I feel like I need to sit down, yeah...with this, when you have to stop you have to stop right then.

(Hopwood and Treloar, 2005 p.640)

Other physical side effects are also commonly described such as flu-like symptoms, insomnia, weight and hair loss, headaches, dysguesia and myalgia as well as upper respiratory and gastrointestinal symptoms (Fraenkel, McGraw, Wongcharatrawee and Garcia-Tsao, 2006; Hopwood and Treloar, 2005; Sheppard and Hubbert, 2006; Taylor-Young and Hildebrandt, 2009; Zickmund *et al*, 2006). Whilst not unusual or unexpected from a physician's point of view, these ongoing side effects can impact on HRQoL in a number of ways. They compromise employment opportunities and contribute to absenteeism (Hopwood and Treloar, 2005); they affect physical appearance and changes in demeanour which result in altered perceptions by others (Sheppard and Hubbert, 2006); and they also contribute to social isolation (Janke *et al*, 2008). The persistence of these symptoms throughout the course of treatment, and the unpredictability of onset were also significant factors contributing to the reduced HRQoL experienced (Fraenkel *et al*, 2006). In addition, participants often felt under-prepared for the severity of these side-effects, noting a discrepancy in the information provided pre-treatment and their actual experience, commenting that the quantity of information often did not equal the quality (Fraenkel *et al*, 2006; Sheppard and Hubbert, 2006). Interestingly, Treloar and Hopwood (2008) explored the concept of unrealistic optimism within the field of preparation for HCV treatment, noting that patients often felt information provided pre-treatment was not relevant to them as they judged themselves to be at low risk of developing severe side-effects. Could this feeling of being under-prepared expressed by individuals going through treatment be partly accounted for by an unrealistic expectation of what was to come?

Although narratives from participants who have experienced serious side effects and intensely emotional journeys through treatment are common within the literature, there are also examples of individuals finding things much better than expected, illustrating the diversity of patient experience:

About the worst thing I've experienced was some nausea...but it's not near what they said.

(Groessler *et al*, 2008 p.1962)

The neuro-psychiatric side-effects of pegylated-interferon have been repeatedly and comprehensively described (e.g. Raison, Demetrashvili, Capuron and Miller, 2005), and a general awareness of the risks of mood swings and depression is found amongst patient groups (Fraenkel *et al*, 2006; Sheppard and Hubbert, 2006). Whilst the impact of these symptoms on continued treatment adherence has been studied (Mathes, Antoine and Pieper, 2014), the impact on the quality of day-to-day life has been less reported. Perhaps unsurprisingly, a significant impact of any neuro-psychiatric symptoms experienced is felt on those closest to the patient, with depression and mood swings taking a toll on spousal and family relationships (Sgorbini *et al*, 2009; Taylor-Young and Hildebrandt, 2009). Janke *et al* (2008) described participants' depression, anger and irritability, which resulted in difficulties controlling their actions and what they were saying to others, subsequently affecting family relationships and in some cases expressing a notion that they had lost their sense of self:

I stayed stuck on mean and evil... Once I get that shot [interferon], I try and avoid him [grandson], because I know how mean I'm going to get. I'm going to be hollering at him, which is why I do not want to do that. But looks like everything he does aggravates me...

(Janke *et al*, 2008 p.496)

Hopwood and Treloar (2005) note that patients may often group numerous psychiatric adverse effects under the label of depression as this is the side-effect they had been warned about. However, they found participants in their study describing quite different treatment-induced mood disorders such as obsessional thoughts and generalised anxiety. Often these symptoms became increasingly severe and sustained as treatment continued, having a major impact on quality of life:

It was like an uncontrollable sense of anger. I'm surprised I have any friends left. I literally just completely withdrew. I really didn't want to deal with people in any way, shape or form. I mean, I felt anxiety and I felt very angry and I was starting to lose control.

(Fraenkel *et al*, 2006 p.150)

Due to the knowledge that depressive symptoms could be a common side effect, Zickmund *et al* (2006) also highlight that participants who were not affected, often feared that it would emerge at some point, living with a sense of lingering inevitability.

2.3.9.3 Social isolation

In addition to the previous discussion of social isolation occurring following HCV diagnosis, the treatment itself can also contribute to this (Fraenkel *et al*, 2006; Janke *et al*, 2008). Taylor-Young and Hildebrandt (2009) describe treatment-related fatigue and lack of energy presenting barriers for participation in social events, but also physical symptoms such as heat-intolerance and photophobia preventing their participant leaving the house during the summer months. Examples of voluntary isolation are also evident within the literature, with some participants describing feeling 'shut in' during treatment, and acknowledging that the only way to obtain breathing space was by withdrawing from family and friends (Sgorbini *et al*, 2009). A mixed-methods study in America highlighted that over half of their 200 study participants reported difficulty attending social functions. However, the qualitative data exposed that this was often in a conscious effort to avoid having to explain or discuss their situation (Manos, Ho, Murphy and Shvachko, 2013), effectively maintaining a voluntary but enforced social isolation during therapy. Further consequences of this are alluded to by Sgorbini *et al* (2009), who describe participants struggling to maintain a meaningful life whilst isolated from their usual social networks. Of interest, provider-imposed requirements for treatment have also been noted to adversely affect social interaction, as a reduction in alcohol and illicit drug use often necessitates a reduced interaction with friends and acquaintances (Zickmund *et al*, 2006).

2.3.9.4 Coping during treatment: resilience and support

With insights into the lived experience of treatment and its side-effects, understandings into how these symptoms are managed and strategies for coping are also illuminated. Hopwood and Treloar (2008) focused on resilience theory, describing participants drawing on past experience of drug dependence, their history and experience of living with a chronic illness and challenges and lessons learned from a socially disadvantaged past. This theory is borne out in other studies, with examples of patients undergoing HCV treatment relating their use of anger management

techniques learned at an alcohol treatment centre (Taylor-Young and Hildebrandt, 2009), and eschewing HCV support groups in favour of more familiar 12-step programmes previously attended such as Alcoholics Anonymous (Sheppard and Hubbert, 2006). More recent reports from the UK also support this theory, highlighting and commenting on resilient coping mechanisms for those undergoing interferon-based therapy (North *et al*, 2014; Ware, Davies, Rowse and Whittaker, 2015).

In addition to resilience, support from friends and family is also a key factor in adherence to and continuation of treatment (Chapman and McManus, 2012; Sgorbini *et al*, 2009; Swan *et al*, 2010). Recurrent reports of strong family support are not uncommon in the literature (Jiwani *et al*, 2013; Manos *et al*, 2013; Sheppard and Hubert, 2006), with the practical support offered by family members and spouses being highly valued and significantly easing the burden of treatment for patients (Sgorbini *et al*, 2009, Swan *et al*, 2010). This can create strain, stresses and challenges to family relationships, however. Sgorbini *et al* (2009) interviewed patients currently undergoing HCV treatment and their partners, and described altered relationships with family and friends and a deterioration of social networks. Research conducted with social workers confirms that relationships are often challenged by treatment, and interventions that include couple and family work are commonly undertaken and can become the core function of the social worker in HCV treatment centres (Mouton, 2011). There is a mixture of positive and negative experiences of friend and family support during therapy described, however the negative aspects are more widely discussed within the literature and appear far more pertinent and relevant to patients and family members themselves.

There is an assumption that adequate social support is important for HCV treatment success. However, very few qualitative studies have examined this relationship. Blasiole *et al* (2006) conducted a mixed-methods study and described lower social support being associated with higher anxiety, more psychiatric diagnoses and lower psychological well-being generally. In addition, they reported patients with lower social support were more likely to report severe physical side-effects during treatment. The relevance of this relates to the perseverance with and adherence to therapy. If

patients with lower social support perceive their symptoms as more intense and frequent, affecting HRQoL to a degree which becomes intolerable, they may be more likely to discontinue therapy early leading to poorer outcomes. The importance of an individual's support system being as fully informed and educated regarding side-effects and what to expect during a period of therapy also echoes through a number of studies (Manos *et al*, 2013; Ware *et al*, 2015):

"Your support network need to be told she could potentially do A, B, C or D, are you prepared to support her through this [...] don't just treat the patient, treat the support network"

(Ware *et al*, 2015 p.998)

2.3.9.5 The persistence of side-effects

Persistent side-effects from interferon-based treatment are reported by both those who achieve an SVR, as well as those who do not respond (Hopwood, 2013). They include both physical and psychiatric problems, and due to their endurance post-SVR are not commonly investigated or even acknowledged by many medical professionals, leaving individuals feeling disregarded and uncared for (Hopwood, 2013; Manos *et al*, 2013). The effect on HRQoL is also marked, increasing anxiety and depression, delaying return to work and the ability to work effectively, and affecting personal and sexual relations (Hopwood, 2013).

2.4 Discussion

2.4.1 The limitations of quantitative PROMs

As the experience of illness and treatment from the patient perspective continues to gain importance, this chapter has endeavoured to demonstrate the value of considering PROMs from a variety of sources. Within the field of HCV, PROMs are most frequently collected using self-completed questionnaires, which generate quantitative data that can be compared to population norms, healthy controls or other specific conditions (Foster, 2009). The most frequent PROM obtained is HRQoL, which has been shown to be significantly lower in individuals with HCV than population norms (see table 1), due to a complex multifactorial cause. During treatment for HCV, a further transient reduction in HRQoL has historically been observed (Bernstein *et al*, 2002; Bianchi *et al*, 2000; Hassanein *et al*, 2004; Hollander *et al*, 2006; Hunt *et al*, 1997;

Marcellin *et al*, 2011; Mathew *et al*, 2006; McHutchison *et al*, 2001; Rasenack *et al*, 2003; Sinakos *et al*, 2010; Vera-Llonch *et al*, 2013; Ware *et al*, 1999; Younossi *et al*, 2014a; Younossi *et al*, 2014b) followed by improvement if an SVR is achieved (table 2). Such reports describing the health status of individuals at specific time-points provide valuable data to satisfy drug licensing requirements, and provide accessible insights into HRQoL. These are beneficial for assessing cost utility and thus the economic benefits of an intervention.

However, much of this evidence comes from large multicentre RCTs, whose participants are often unrepresentative of the larger HCV population, undermining ecological validity and generalisability (Britton, McKee, McPherson, Sanderson and Bain, 1999; Van Spall *et al*, 2007). To illustrate this point, Beinhardt *et al* (2012) examined whether selection bias was observed within their clinical centre for patients who underwent HCV treatment through an RCT. Those enrolled to an RCT had less advanced liver disease, less frequent history of psychiatric disorders and were less likely to be prescribed opioid-substitution therapy compared with those receiving routine care, which was largely driven by the studies exclusion criteria. In another example, in a large RCT for patients being treated with telaprevir, Vera-Llonch *et al* (2013) reported that trial participants' baseline EQ-5D scores were actually higher than published US population norms making them not only unrepresentative of the HCV population, but of the general population as well¹⁷. These types of selection bias conspire to present evidence for HRQoL obtained under 'ideal' conditions, with far fewer reports on the effect in 'real-world' populations with HCV.

In addition to concerns regarding generalisability, there are also methodological difficulties with psychometric questionnaires measuring HRQoL. Individuals with low literacy skills are frequently excluded from studies that develop and validate self-completed questionnaires (Jahagirdar, Kroll, Ritchie and Wyke, 2013). This has particular relevance within the field of HCV, as it is estimated that up to 90% of those infected in Scotland are current or former PWID (Hutchinson *et al*, 2006) who typically

¹⁷ One possible contributing factor towards this was the frequency and breadth of cytochrome P450-associated drug interactions with first generation protease inhibitors, resulting in de facto exclusion of patients with multiple comorbidities from clinical trials due to higher levels of poly-pharmacy (Talavera Pons, Lamblin, Boyer, Sautou and Abergel, 2014).

fall into this category. The use of psychometric questionnaires has not therefore been validated in actively substance-using populations (Dalgard *et al*, 2004). Further methodological difficulties including the complexity of choosing the correct tool, the lack of standardisation across a condition-specific field, and the extent to which the chosen tool covers the concept being investigated have also been reported (Refolo, Minacori, Mele, Sacchini and Spagnolo, 2012).

The extent to which a tool covers all the concepts being addressed, or more accurately fails to cover, can lead to a combination of different PROMs being used within the same study. For example, recent trials using DAAs in the treatment of HCV administered four separate questionnaires to their patients: the SF-36 - a generic HRQoL survey; the CLDQ-HCV - a disease-specific HRQoL survey; the FACIT-F used to assess the impact of fatigue; and the WPAI:SHP investigating impairment in daily activities and work productivity (Younossi *et al*, 2014a; Younossi *et al*, 2015; Younossi *et al*, 2016b; Younossi *et al*, 2016c; Younossi *et al*, 2016d; Younossi *et al*, 2016e). The sheer volume of paperwork involved in completing these questionnaires, and the time and concentration required to do so calls into question the quality of the information collected. In addition, questionnaires may not capture the most pertinent concerns of the patient. These instruments do not elucidate what strategies are employed by people to cope with any decrements to HRQoL they may be experiencing, or explore the impact on behaviour and functioning in wider society. The burden of illness is reduced to figures which may or may not show statistical and clinical significance, but the patient experience, and the patient voice, may be lost in the process.

2.4.2 The value qualitative insights

In addition to the wealth of literature surrounding the quantitative analysis of HRQoL in patients with HCV, there is also a body of qualitative research providing more in-depth focus into the lived experience of the disease (Miller, McNally, Wallace and Schlichthorst, 2012). These studies give a recognisable voice to the everyday challenges experienced by individuals living with the virus. They provide insights into the multidimensional nature of fatigue (Glacken *et al*, 2003); demonstrate the impact that concerns over onward transmission can have (Conrad *et al*, 2006); and explore the pervasive and consuming nature of stigma (Butt *et al*, 2008; Conrad *et al*, 2006; Faye

and Irurita, 2003; Fraser and Treloar, 2006; Fry and Bates, 2012; Hill *et al*, 2015; Paterson *et al*, 2006; Zickmund *et al*, 2003).

The qualitative literature complements the quantitative HRQoL data, and also aids its interpretation. For example, the insights gained into how HCV is viewed as a chronic illness help explain the variation in HRQoL observed in quantitative studies. If living with HCV is considered along a chronic illness continuum, individuals who have achieved varying degrees of HCV-accommodation in their lives will also therefore exhibit varying responses to psychometric questionnaire temporal snapshots. Without this insight, it could be argued that compiling these responses and effectively reporting a 'mean value' has limited relevance and clinical application. Indeed, this approach also masks the disparity of reactions to diagnosis amongst PWID and other groups illuminated by the qualitative paradigm. A lower HRQoL is not necessarily *experienced* in the same way by all those it affects, which may have significant implications for engagement in treatment services. Further, without accounting for the social stigmatisation HCV elicits (Paterson *et al*, 2007), the findings of most questionnaire-based HRQoL research are left open to conjecture.

Qualitative exploration into the experience of undergoing a period of HCV therapy has also proved invaluable. These richer and more personalised accounts of treatment assist a deeper understanding of why certain side-effects may lead to poor adherence and treatment discontinuation i.e. the fatigued patient is not just 'tired', their HRQoL is severely compromised due to emotional, physical and psychological exhaustion (Glacken *et al*, 2003). This qualitative work also highlights the strategies used to cope with any side-effects experienced, for example exploring the importance and mechanics of support. Without this body of work, the significance and relevance of data from HRQoL questionnaires would remain unclear, and the patient voice silenced.

Qualitative studies give a recognisable voice to the decrements and improvements in HRQoL described in the quantitative work in addition to revealing more nuanced and deeper insights which also have important clinical significance. The two bodies of research are therefore not only complementary, but essentially interconnected. The

depth of understanding of the burden of illness is absent unless qualitative accounts of the lived experience are reviewed concurrently alongside quantitative research.

2.4.3 A significant gap

With this in mind, it is significant that there has been a relative absence of published qualitative studies focused on the experience of being HCV positive since the start of the DAA era. Exploration of the lived experience of HCV within an age of constantly and rapidly improving treatment options is essential if a contemporary understanding of the disease is to be achieved. It is reasonable to suggest that the significant pharmacological developments being witnessed may influence how HCV is being understood and experienced by those living with the virus. For example, are perceptions of the illness changing in response to the evolution in HCV therapy, or do constructions of HCV as a chronic condition and the embodied experience remain unchanged? There appears an incongruity in continuing to apply chronic illness models to a disease that is now cured in over 90% of those who are able to access DAA treatment. However, data are sparse. The search strategy utilised for this review found only two publications focused on the experience of being HCV positive with data collected during the DAA era. One of these articles focused exclusively on the Aboriginal Australian community (Treloar *et al*, 2016), and the other restricted itself to an examination of the experience of HCV-related fatigue (Zalai *et al*, 2016).

The experience of undergoing HCV treatment in this new era of therapy has also received limited attention. Whilst the quantitative literature continues to report contemporary data on HRQoL with new treatment regimens (e.g. Younossi *et al*, 2014a; 2014b; 2014c; 2014d; 2016a; 2016b; 2016c; 2016d; 2016e; 2016f; 2016g), qualitative insights into these therapies lag behind. Only three studies were identified which provided qualitative exploration of HCV treatment since the arrival of the DAAs (Evon, Golin, Bonner, Grodensky and Velloza, 2015; Rasi *et al*, 2014; Sublette, Smith, George, McCaffery and Douglas, 2015). As these studies were all conducted with individuals taking interferon-based triple therapy, they were also of more historical curiosity than contemporary relevance, given such regimens are now largely obsolete in Western nations. To date, there are no published qualitative explorations of individuals receiving interferon-free regimens, which are now standard of care for

many individuals with HCV living in Scotland (HIS and NHS National Services Scotland, 2015a). Without these richer and more tangible patient narratives, a deeper understanding of the lived experience of a period of interferon-free HCV treatment is absent.

2.4.4 Research questions

The lack of contemporary qualitative research focused on the lived experience of HCV and its treatment inform the three research questions which lie at the heart of this thesis.

Research Question 1:

How is living with hepatitis C experienced and understood within the context of a new era of treatment?

Research Question 2:

How adequate do theories of chronic illness remain to the contextual understanding of living with hepatitis C?

Research Question 3:

How is interferon-free treatment for hepatitis C experienced and contextualised?

The remainder of this thesis aims to address these questions through empirical research. The following chapter details the methodology and methods employed, with subsequent chapters focused on the analysis and discussion of the collected data.

Chapter 3

Methodology and methods

3.1 Introduction

This chapter aims to provide a comprehensive overview of the study methodology, the study design, and the methods through which the empirical data were generated. The terms methodology and methods are often poorly defined within the literature. For clarity, I employ the term methodology to encapsulate the ontological and epistemological positions underpinning this study, in addition to the specific theoretical perspective of social phenomenology upon which it is based (Wilson, 2002). By methods, I refer to the practical activities of research, the actions which have been termed the 'nuts and bolts' of research practice (Carter and Little, 2007). The chapter begins by stating the rationale for employing a qualitative approach, making clear the ontological and epistemological beliefs which underpin this inquiry. Discussion of the overarching theoretical perspective of social phenomenology follows, including a detailed account of how this theoretical framework was selected. Barbour (2014) notes that for the novice qualitative researcher, the wealth and variety of theoretical traditions, in addition to the existence of several variants of virtually every approach, makes navigating the literature a confusing pastime. The work is rarely laid out in an organised fashion, with the inconsistent use of terminology between different texts adding to the confusion (Crotty, 1998). I have therefore chosen to describe my journey through the literature, as explaining my thought process and charting the steps that guided my arrival at the door of social phenomenology should provide a clear and compelling justification for its appropriation. This is also the reason I revert to writing in the first person for sections of this chapter.

The second half of this chapter provides a rationale and description of the study design and methods utilised, focusing on the practicalities of the research process. These practicalities include sampling strategy, participant recruitment, data generation, data handling and the approach to analysis. The ethical considerations which these activities necessitate are then discussed. These applied aspects of the research process are fundamentally based on the overarching theoretical perspective of social

phenomenology. By demonstrating how the research methodology shaped and guided the methods chosen, a coherent and logical rationale is presented for the research design, enhancing the rigour and trustworthiness of this endeavour.

To begin, however, it is necessary to briefly justify my decision to pursue a qualitative approach to data collection, and then examine the ontological and epistemological positions this decision necessitates. In the interests of clarity, I intend to address the inconsistent use of terminology throughout this chapter by making explicit my understanding of theoretical and methodological terms where necessary, in order to avoid being misconstrued.

3.2 Methodology

3.2.1 A qualitative approach

The research questions posed within this study aim to explore how the rapid evolution in the treatment of HCV is shaping the way this disease is experienced, understood and realised by those it affects. As such, it aims to elicit the 'lived experience' of being HCV positive rather than providing a quantitative assessment of health-related quality of life. Extensive justification for this approach has been made within the previous literature review (chapter 2). Events, or phenomena (such as lived experience), are the result of multiple factors coming together and interacting in complex and often unanticipated ways (Corbin and Strauss, 2008). As such, a methodology that is able to celebrate this complexity, and accept richness, nuance, depth and context within the analysis is a vital consideration (Mason, 2002). As the research questions have been formulated primarily from the lack of contemporary qualitative research in this area, it is unsurprising that a qualitative methodology appears most suited to answering them (Bryman, 2012).

3.2.2 Ontology and epistemology

The choice of a qualitative approach to research brings with it some ontological and epistemological considerations. By ontology, I refer to theories about the nature of reality, or as Corbin and Strauss (2008) phrase it, our assumptions about the world. By epistemology, I am referring to theories of knowledge and how we come to know the world (Barbour, 2014). Ontologically, I am a realist. I believe that there is a real world

that exists independently of our perceptions, theories and constructions of it. For example, I believe there are trees, animals and mountains irrespective of whether human beings are conscious of them. However, I do not accept that this real world is objectively knowable. The trees, animals and mountains only become meaningful when meaning-making beings make sense of them (Crotty, 1998) i.e. the objects only *become* trees, animals and mountains when consciousness is directed towards them. As meaning-making is a subjective process, this naturally leads to the acceptance that there are many different but equally valid perspectives on reality (Maxwell, 2012). The acceptance of different perspectives on reality should be distinguished from a belief in multiple realities as championed by constructivists and grounded in a more relativist ontology. Believing in valid and differing perspectives of the real world as subjectively constructed by meaning-making individuals is not the same as accepting that those subjective constructions actually constitute reality, and that a 'real world' does not exist.

With this in mind, I position myself as a critical realist, a perspective which retains an ontological realism while accepting a *form* of epistemological constructivism (how we come to know and understand the world is inevitably a construction from our own perspective and standpoint) (Maxwell, 2012). As Crotty (1998) notes, realism in ontology and constructivism in epistemology turn out to be quite compatible. An early proponent of this ontological/epistemological union was Herbert Blumer (1900-1987), the leading figure in the symbolic interactionist approach to research. Although the 'constructivist' term was not available to him at that point, Blumer argued that an empirical world exists as something available for observation and study, and although this world exists to us in the form of human conceptions of it, this does not shift 'reality' from the empirical world to a realm of imagery and conception (Blumer, 1969). In other words, the conceptions formed of the world are all equally valid, but are, and remain, perspectives of the empirical world. How we construct these perspectives on reality became the key focus of my journey through the theoretical literature, which ultimately led to the door of social phenomenology.

Social phenomenology as an approach to research builds on philosophical thought and traditions nurtured in early twentieth-century Europe, and then developed in America

following the emigration of its key proponent Alfred Schütz (1899-1959) in the wake of Hitler's Austrian Anschluss. It is therefore prudent to pause and reflect on the foundations of this approach prior to examining social phenomenology itself, as a more complete appreciation of social phenomenology's fit to this study can be expounded by examining its roots. In doing so, I take the opportunity to explain my reasoning as to why other phenomenological approaches which were considered and appraised were ultimately side-lined in favour of Schütz's perspective.

3.3 Phenomenology

3.3.1 Phenomenologies

Phenomenology is a philosophical approach to the study of lived experience founded by the German philosopher Edmund Husserl (1859-1938) at the start of the 20th century (Smith, Flowers and Larkin, 2009). It was launched under Husserl's banner that we should go 'back to the things themselves', meaning a focus on describing the first person account of immediate experience, and allowing that lived experience to speak for itself. At the core of phenomenology lies the attempt to describe and understand the essence of phenomena¹⁸ as experienced by the individuals who have lived through them (Wojnar and Swanson, 2007). This descriptive approach to phenomenology was later challenged by Martin Heidegger (1889-1976), a former student of Husserl, and later by other existential phenomenologists, whose interpretive stance set them apart from many of the fundamental tenets of the Husserlian school. However, the Husserlian tradition also endured, and was elaborated on and developed by, amongst others, Alfred Schütz, who framed phenomenology from a sociological perspective. As different scholars employed divergent philosophies under the phenomenology banner, various strands arose with differing epistemological and ontological perspectives. As such, using the term phenomenology as a singular entity is perhaps misleading, and the plural term 'phenomenologies' may be better employed (Lawler, 1998).

¹⁸ Where a phenomenon is anything that presents itself (McConnell-Henry, Chapman and Francis, 2009).

3.3.2 Husserl

Originally a mathematician, Husserl became disenchanted and disillusioned with the natural sciences as a means of studying human experience, and developed the philosophy of transcendental¹⁹ phenomenology in response (McConnell-Henry, Chapman and Francis, 2009). He opposed the view that empirical science was the sovereign arbiter of truth, and saw phenomenology as a way of returning to and exploring the reality of life and living, of going 'back to the things themselves' (Tuohy, Cooney, Dowling, Murphy and Sixsmith, 2013). Husserl introduced the concept of the *lebenswelt*, or 'life-world', meaning the world as it is immediately experienced (Wilson, 2014), and claimed that the life-world was not readily accessible, as it constituted that which is taken for granted and those things which are common sense (and therefore go largely unnoticed) (Koch, 1995). Study of the life-world therefore explores what an experience is like 'pre-reflectively', focusing on that which is experienced in the consciousness of the individual (Smith *et al*, 2009). This approach was rooted in the philosophical dogma of the day, and elaborated from the mechanistic model of the mind-body split, known as Cartesian duality (Koch, 1995). It is prudent to explore some of the critical concepts of transcendental phenomenology, as a deeper understanding can serve to help illuminate the contrasting hermeneutic paradigm of Heidegger, and discussion of the concept of bracketing will provide a rationale for the rejection of pure transcendental phenomenology in this study.

3.3.2.1 Intentionality

A central tenet of phenomenology is intentionality. Husserl held that we are never simply conscious, but instead, our consciousness is intentional in that it is always directed or pointed toward something (LeVasseur, 2003). Crotty (1998) describes intentionality as the relationship between conscious subjects and their objects; consciousness is always consciousness *of* something, and the objects always *mean* something to someone. These objects can be real, imaginary or conceptual, or consciousness can also be directed at the object of itself e.g. our own emotions and thoughts (Hein and Austin, 2001). Phenomenological inquiry therefore focuses on that which is intentionally experienced in the consciousness of the individual (Smith *et al*,

¹⁹ This branch of phenomenology is also referred to as Descriptive Phenomenology, Husserlian Phenomenology and Eidetic Phenomenology

2009). That is, the first-person subjective experience which occurs independent of their actual relationship with the external world. The context of experience is disregarded in transcendental phenomenology and the focus is on the experience alone (Tuohy *et al*, 2013). For Husserl, intentionality is the key to understanding human experience (Earle, 2010).

3.3.2.2 Bracketing

Despite his disillusionment with the natural sciences as a means of studying human experience, Husserl remained a positivist and strived for objectivity and neutrality as he believed this was the only way of assuring methodological trustworthiness (Fleming, Gaidys and Robb, 2003). Bracketing²⁰, a fundamental methodological principle of transcendental phenomenology, was Husserl's approach to ensuring the researcher does not influence the participants' understanding of the phenomenon under investigation, as in order to understand the nature of phenomena all prejudice must be eliminated (Hamill and Sinclair, 2010). It aims to ensure researchers' preconceptions are held in abeyance and assumptions are not allowed to impose understanding (Hamill and Sinclair, 2010). Bracketing seeks to approach events with an investigative mind left deliberately open, consciously trying to 'bracket out' preconceived ideas and assumptions as the researcher is not studying their own awareness and reflections, but the awareness and reflections of the study participants (Willis, 2001). By acknowledging, examining and putting aside one's beliefs, the researcher should attain native data (McConnell-Henry *et al*, 2009) and achieve the transcendental ego: the consciousness Husserl described as necessary for the understanding of pure phenomenal experience (LeVasseur, 2003). This is an etic approach which strives for objectivity (Hamill and Sinclair, 2010), and is often distilled to simply having a fresh look at the world, leaving our usual understandings²¹ in abeyance (Crotty, 1998).

²⁰ Also termed phenomenological reduction, eidetic reduction or epoché.

²¹ Exactly what should be bracketed has been a source of discussion within the literature for a number of years, with the terms assumptions, judgements, biases, beliefs, presuppositions, experiences, issues, knowledge, perceptions, preconceptions and pre-understandings all used within this context (Hamill and Sinclair, 2010).

The notion of bracketing was subsequently criticised and rejected by Heidegger and other existential phenomenologists (LeVasseur, 2003), who espoused the view that understanding is never without presuppositions (Earle, 2010) and that understanding is already there, and cannot, nor should not, be divorced from our thinking (Smythe, Ironside, Sims, Swenson and Spence, 2008). They also accused Husserl of betraying his own doctrine of intentionality, as this was contradicted by the notion of bracketing (LeVasseur, 2003). From a practical viewpoint, Husserl did not offer a method by which bracketing could be achieved, and doubts around whether it is attainable have permeated the literature. Is it truly possible to suspend all beliefs, thoughts and influences when we are embedded in a world of meaning? Hamill and Sinclair (2010) note that having an awareness of personal feelings and preconceptions is a prerequisite for setting them aside. However, how can one be certain that these have been brought to the level of consciousness and acknowledged? Also, even if the researcher were successful in bracketing, what of the participants? Does the fact that participants do not consciously bracket their own conceptual framework when narrating their experience mean that our knowledge is based on a fundamentally flawed and skewed understanding? (LeVasseur, 2003).

The impetus for this research project came from my experience of working within the field of HCV treatment over a number of years. The accumulated hours of practical clinical experience, the associated clinical knowledge, and the countless interactions and consultations with patients both before, during and after HCV treatment confers on me a wealth of presuppositions, perceptions and beliefs. The feasibility of attempting to 'bracket out' this extensive experience is questionable, particularly for a novice researcher, and the relative success or failure of such an undertaking would have significant implications for the trustworthiness and credibility of this piece of work. In addition, I conducted the literature review detailed in chapter two prior to this exploration of qualitative methodologies. Hamill and Sinclair (2010) note that delaying the literature review until after data collection and analysis can assist the achievement of bracketing, by ensuring themes known to exist in the literature do not dominate question phrasing or analytical techniques, with other authors also suggesting a literature review should be avoided if Husserl's phenomenology is subscribed to (McConnell-Henry *et al*, 2009). The most pertinent argument against the

use of transcendental phenomenology, however, is the philosophical one. Annells (1996) describes the person and the world as co-constituted in an indissoluble unity, and as such “*man [sic] makes sense of his world from within his existence and not while detached from it*” (Annells, 1996 p.706). It is with this in mind that we turn to the development of Heidegger’s hermeneutic phenomenology.

3.3.3 Heidegger

The German philosopher Martin Heidegger (1889-1976) was a student of Husserl. However, with his seminal work *Sein und Zeit* (Being and Time) he moved radically away from Husserl’s phenomenological approach (Earle, 2010). The process of bracketing provides information that is epistemological, rather than ontological in nature, i.e. you can know something through description, but cannot understand it or derive meaning from it (McConnell-Henry *et al*, 2009). Heidegger travelled from the epistemological emphasis of Husserl to an emphasis on the ontological perspective (Earle, 2010), believing the outcome of phenomenological research should be understanding and meaning through interpretation rather than a purely descriptive science (McConnell-Henry *et al*, 2009). He replaced the concept of knowing with that of understanding. Understanding was not possible because of knowing, it was possible because of relationships (Fleming *et al*, 2003).

Heideggerian phenomenology²² is based on the perspective that the understanding of individuals cannot occur in isolation from their culture, social context, and the historical period in which they live (Wojnar and Swanson, 2007) therefore challenging two notions of Husserl: firstly, that meaning can be seen in terms of representation of an independent reality, and secondly, that theory can be generated from the standpoint of an observer standing outside the situation (the etic position) (Koch, 1995). Heidegger held that consciousness could not be separated from what he termed *in-der-Welt-sein*, or being-in-the-world, a term used to emphasise the temporary, existential and relational basis of our daily lives and understanding of the world (Robertson-Malt, 1999). Because of this, the bracketing of prior conceptions and knowledge was unattainable. We are necessarily embedded in an historical

²² Also referred to as Existential Phenomenology, Interpretive Phenomenology and Hermeneutic Phenomenology within the literature

context (LeVasseur, 2003). This key tenet of Heideggerian phenomenology he termed *Dasein*, or 'being there', emphasizing that individuals cannot abstract themselves from various contexts that influence their choices and give meanings to lived experience (Wojnar and Swanson, 2007). These experiences are based on our context of the world, and as humans we cannot be separate from our contexts (Miles, Francis, Chapman and Taylor, 2013). Central to the notion of *Dasein* is its spatiality and temporality. There is an attachment in time and space to culture and history, providing understandings of beliefs and contexts which in turn shed light on the phenomenon of interest: experience is temporally and spatially mediated (Miles *et al*, 2013). This has particular pertinence and relevance for the current study.

The evolution of drug therapy for the treatment of HCV provides the underlying rationale for this study. The experience of living with HCV and undertaking treatment will therefore be temporally bound as the historical context is not static: we are temporal beings in a temporal world (McConnell-Henry *et al*, 2009). For example, being prescribed interferon at a time when this was the best and most effective cure available may be understood and made sense of by an individual in a different way compared with being prescribed interferon at a time when other more efficacious treatments exist. The temporal and spatial context of *Dasein* therefore impacts heavily on both existence and experience. Because of this, Heideggerian phenomenology does not look for generalisable traits, or shared experience, but understands that the truth about an experience, as professed by one person, might differ from that believed by another. Truth is intertwined with perception and context, and there can therefore be multiple truths of a lived experience (Crist and Tanner, 2003; McConnell-Henry *et al*, 2009; Miles *et al*, 2013). This fundamentally contrasts with Husserl's transcendental phenomenological stance which aims to expose the absolute truth through description. Both these positions resonate with my clinical experience. No two patients appear to share a common experience of living with HCV and undergoing treatment. However, there can be similarities and common features of distinctly differing experiences.

3.3.3.1 Heidegger: lost in translation?

On initial reading, the hermeneutic phenomenological philosophy of Heidegger appeared to provide a rational and logical theoretical framework on which to anchor this current research. However, the appropriation of phenomenological theory by nurse researchers has not been without criticism, and the writing of one particular critic in relation to Heidegger is difficult to ignore. John Paley has provided a vocal and enthusiastic challenge to nursing research which claims theoretical justification by citing the tenets of phenomenological philosophy (Paley, 1997; Paley, 2005). He contests the notion that Heidegger's phenomenology has the methodological implications commonly ascribed to it, and ultimately describes the research of 'lived experience' not as a realisation, but rather as a betrayal of Heidegger's philosophy (Paley, 1998). Paley constructs his argument by returning to *Being and Time*, Heidegger's seminal work, and unpicking the common assumptions made by researchers who claim to be undertaking 'Heideggerian phenomenological research'. Primarily, Paley argues that research into lived experience would be anathema to Heidegger, as he explicitly disowns the concept (Paley, 2014). Paley contends that study of the lived experience is always an attempt to access the subjective experience of a phenomenon, not the objective factual account of what actually happened. For example, within this study the objective factual account may be that an individual was diagnosed with HCV, and the subjective experience of that would be the thoughts, meanings, interpretations, emotions and understandings involved. This understanding of a subjective/objective distinction aligns with the Cartesian duality that Heidegger explicitly rejected in favour of his concept of being-in-the-world (Paley, 2014).

"Being-in-the-world cannot be broken up into contents which may be pieced together"

(Heidegger, 1962 p.53)

Reflective recollections of 'lived experience' are therefore not possible. Retrospective subjective experience has no place in Heidegger's work as it reverts to the very dualism he is attempting to dismantle. He does not accept it exists (Paley, 2014). Paley is not the only scholar to critique nurses' interpretation and utilisation of phenomenology as a method for undertaking qualitative research. Crotty (1996) asserts that much of the nursing research that cites a phenomenological foundation has little basis in *pure*

phenomenology as described by its founding philosophers. Instead, he described much of what is claimed as phenomenological research (particularly that emanating from North America) to be a hybrid of symbolic interactionism and humanistic psychology, providing third-person subjective description of phenomena, rather than a critical examination of the phenomena themselves (Barkway, 2001). As such, Crotty (1996) makes a distinction between 'European phenomenological research' and 'new phenomenological research' emanating from the English-speaking world (primarily North America), and implicitly implies inferiority in the latter. The American psychologist Giorgi (2000) offers a spirited response to this argument, agreeing with Crotty that there are two phenomenologies, but terming them 'philosophical' and 'scientific', and in doing so highlighting the fact that neither Husserl nor Heidegger intended to develop research methodologies, their interests being most firmly rooted in the study of philosophy (Miles *et al*, 2013). Indeed, Giorgi (2000) argues that if nurse researchers were to adhere to *pure* phenomenology they would be practising philosophy, and not contributing to 'nursing or caring' scientific work which is surely their original intention.

After reviewing the phenomenologies of Husserl and Heidegger, and exploring the criticism levelled at the appropriation of these philosophies within nursing research, I felt paralysed. The basic aim of phenomenology to 'go back to the things themselves' and describe and understand phenomena as experienced by the individuals who have lived through them is clearly appealing and appropriate for this study. However, how could I justify the appropriation of either transcendental or existential phenomenology after highlighting the issues discussed above? Further reading led to a possible answer.

3.3.4 Schütz and social phenomenology

Alfred Schütz (1899-1959) was an Austrian philosopher and economist, who was greatly influenced by the work of sociologist Max Weber. Although impressed with Weber's theory of social action, Schütz sought to overcome what he perceived as its weaknesses by integrating ideas from philosophers such as Husserl. In doing so, he approached phenomenology from a sociological perspective (Ajiboye, 2012) which resulted in his seminal text *The Phenomenology of the Social World* (Schütz, 1967).

Schütz's social phenomenology is a descriptive *and* interpretive theory of social action that explores subjective experience and the way in which meaning is socially constructed (Fereday and Muir-Cochrane, 2006). It examines how mundane understandings of social life are constituted and organised, both in face-to-face interaction and in more remote contexts (Levesque-Lopman, 1988). He emphasised the profound impact of social interaction in establishing meanings in the world. Thus, whilst greatly influenced by Husserl's phenomenology, he opposed one of his basic tenets that intentional consciousness is the driving force in constituting an object's meaning (Shaw and Connelly, 2012). In essence, Schütz's main contribution was that the way humans classified and attached meaning to the outside world (or constructed their perspective) was not a purely individual process. Hence, whilst other phenomenological philosophers focused primarily on consciousness, Schütz rotated phenomenology outward to a concern for the inter-subjective social world (Ajiboye, 2012).

Schütz believed that inter-subjectivity was the foundation of all human knowledge and experience, because we do not experience the world alone, we experience it with and through others. People learn about what phenomena mean through an interactive process between past experiences and the projected meanings of others in the world (Shaw and Connelly, 2012). Schütz was not primarily interested in the physical interaction of people (as a more symbolic interactionist approach may be), but in the way they relate to and grasp the consciousness of others and in doing so create a common view of the world (Ajiboye, 2012). Social phenomenology therefore proposes that an inter-subjective world is not a private world, but a relational one that is common to all. Put more explicitly, there are common features among people's subjective experiences of any particular social phenomenon that define its meaning. Schütz termed these common features 'ideal type', a notion drawn from the work of Weber and analogous to the notion of 'essences' in Husserl's work. The ideal type is therefore an objective description and understanding of a subjective experience (Shaw and Connelly, 2012). It is the commonalities that are found in the subjective life-worlds of more than one actor. The importance of the ideal type being grounded in the subjective point of view was paramount to Schütz, however, as this prevented

social reality being replaced by a fictional, non-existent world constructed by the researcher (Fereday and Muir-Cochrane, 2006).

3.3.4.1 *Bracketing revisited*

As social phenomenology therefore seeks objective knowledge through accurate descriptions of subjective experience, it remains rooted in the Husserlian school, and, as such, the notion of bracketing must once again be considered. Husserl viewed 'the natural attitude' (that is, the normally occurring and common-sense meanings that characterize everyday life) as sources of bias and distortion for the phenomenologist, and advocated their bracketing in order to approach phenomena with an open mind (Smith *et al*, 2009). This type of bracketing is often termed the phenomenological epoché. To Schütz, the natural attitude was not a discrete consciousness, but a shared and inter-subjective consciousness which itself should form the basic subject of phenomenological investigation (Silverman and Torode, 1980). He proposed that within the natural attitude, individuals also use a specific bracketing (epoché) which is diametrically opposed to the phenomenological epoché. That is, individuals do not suspend belief in the outer world and its objects. On the contrary, they suspend any doubt in its existence: doubt that the world and its objects might be anything other than how they appear (Levesque-Lopman, 1988). This has been termed *the epoché of the natural attitude*. As researchers, we are also individuals that are part of the inter-subjective natural attitude. Therefore, we too suspend doubt that the world is anything other than it appears. For the social phenomenologist researcher, bracketing must *allow* doubt, or more accurately suspension of belief in the existence of the world as we know it.

Whilst acknowledging the previous discussion of whether bracketing is achievable within Husserlian phenomenology, the discussion of epoché within social phenomenology posits a more practical viewpoint. The suspension of belief in the world as we know it suggests the adoption of a questioning, interrogative and searching attitude. I am not asked to remove all experience, knowledge and expertise I possess from my consciousness, but to acknowledge that this may comprise only one possible account of a phenomena. I am asked to doubt, to suspend belief in what I think I know, and allow the possibility that the world exists in a different way. When

viewed in this way, bracketing becomes a more achievable and realistic goal, moving from a purely philosophical realm to one of practical research methodology.

3.3.4.2 A research method

In contrast to Husserl and Heidegger, Schütz moves phenomenology beyond philosophy and discusses the application of practical method within the social sciences. He proposed three essential postulates to be followed during the research process to ensure the objective ideal type was founded in the subjective meaning of human action (Schütz, 1973 p.43-44 [abridged]):

1. *The postulate of logical consistency: the researcher must establish the highest degree of clarity and distinctness of the conceptual framework and method applied, which must be fully compatible with the principles of formal logic.*
2. *The postulate of subjective interpretation: any model of human action must ground its construction in the subjective meanings the 'actor' had for the action.*
3. *The postulate of adequacy: there must be consistency between the researcher's constructs and those found in the common-sense experience; it must be recognisable and understood by the actors within their life-world.*

These three tenets provide a framework upon which the philosophical underpinnings of Schütz can be used to consider more practical research methods for the current endeavour. My hope is this overview of my journey through the literature supports Schütz's first postulate of logical consistency.

For the current study, the theoretical underpinnings of social phenomenology provide an attractive fit. My realist/constructivist union corresponds well with Schütz's teachings. In addition, the approach encompasses phenomenology's core attempt to describe and understand phenomena as experienced by the individuals who have lived through them (Wojnar and Swanson, 2007) with a sociological perspective into the way that experience is constructed. It moves phenomenology on from a purely philosophical pursuit, to a methodological approach to research that remains committed to understanding lived experience and the ways in which it is constructed.

With this in mind, I will now move on to describe the design of the study, recruitment process and analytical techniques employed.

3.4 Methods

Having made my ontological, epistemological and theoretical positions evident, I now turn to the more practical discussion of methods employed for data generation and analysis. The design of this study incorporated semi-structured in-depth interviews with a purposive sample of HCV positive individuals. A longitudinal element of the study design followed-up a subset of these individuals who subsequently received interferon-free HCV treatment. Previous discussion of the underpinning methodology necessarily guided, informed and justified the study design, in addition to its appropriateness in answering the research questions posed. Methods and methodology are intricately and inextricably connected, and where necessary, discussion will therefore focus on the choice and appropriateness of data collection and analytical techniques as the practicalities of the study design are considered.

3.4.1 Sampling

In qualitative research, sample selection has a profound effect on the overall quality and rigour of the study, yet is often poorly described or justified (Coyne, 1997). This study utilised a purposeful (or purposive) sampling strategy, which involved selecting participants by virtue of characteristics thought to have some bearing on their perceptions and experiences (Barbour, 2014). There was a need, therefore, to think critically about the parameters of the population being studied and choose the sample carefully on that basis (Silverman, 2013). The type of purposeful sampling used was a maximum variation sampling strategy, which will now be described.

3.4.1.1 Maximum variation sampling

Maximum variation is a purposeful sampling strategy that aims to capture and describe central themes that cut across a high degree of variation in the participants. It assumes that common patterns that emerge from great variation are of particular interest and value in capturing core experiences and shared dimensions of a phenomenon (Patton, 2015). As such, the relevance of this approach to the social phenomenological perspective underpinning this study becomes immediately

apparent: this sampling strategy promotes the illumination of Schütz's 'ideal type'. In addition, the variation in characteristics built into the sample allows for meaningful comparisons to be drawn during analysis (Mason, 2002).

The maximum variation sample was constructed by the identification of diverse characteristics of the potential sample population in relation to their experience of HCV and its treatment. The identification of these characteristics was based on personal experience of working with HCV patients as a specialist nurse for a number of years, the literature review undertaken in the process of developing the study's research questions, and reflection on what may constitute 'common-sense' categories (Mason, 2002). The main characteristics identified were:

- *Engagement with specialist HCV care:* Individual experience and understanding of HCV may vary depending on whether participants attended specialist HCV services and engaged with assessment and clinical work-up for HCV treatment. The on-going success of the HCV action plan for Scotland (Scottish Government, 2015a) means there are fewer individuals diagnosed with HCV who remain 'unengaged' with care. These individuals were predicted to be the most difficult and elusive group to recruit.
- *Date of HCV diagnosis:* Following the arrival of DAAs in clinical practice, and the significant improvements in treatment options available for people with HCV, individual variation in response to HCV may exist based on when a diagnosis was made. As the first DAAs became available for treatment in Scotland in 2011 (Scottish Medicines Consortium, 2011b), that year was taken as marking the start of the new era in drug therapy.
- *Mode of acquisition:* The manner in which HCV was contracted may influence and inform the experience of living with the virus. Whilst injecting drug use continues to be the predominant route of viral transmission (Palmateer *et al*, 2013), the study did not aim to focus exclusively on this cohort.

- *HCV treatment history:* Exposure to previous interferon-based treatment may influence and inform perceptions of HCV and new drug therapies.
- *Degree of liver disease:* The severity of liver disease has been repeatedly shown to affect quantitative measures of HRQoL (Orr *et al*, 2014). The study therefore aimed to include participants who identified as cirrhotic, and those who did not.

In addition to these factors, gender and ethnicity were also incorporated into the maximum variation sample. This was not an attempt to produce a sample that was representative of the wider population, but in order to reflect diversity and provide as much potential for comparison as possible (Barbour, 2014). Markers of socioeconomic status were not included in the maximum variation sample, as HCV is known to disproportionately affect populations who are marginalised and underserved (Public Health England, 2016). As such, it was predicted that the majority of participants would be of lower socioeconomic status, but that the parameters of the maximum variation sample would naturally draw in individuals from other socioeconomic backgrounds. Demographic data concerning living arrangements and employment were collected to examine this.

3.4.1.2 Inclusion and exclusion criteria

The following inclusion criteria were applied to the sample:

- Participants must be living within Edinburgh and the Lothians, and have been infected with HCV for at least six months to allow for any spontaneous clearance of acute infection (Seeff, 2002).
- They must be aged 16 years or over, and able to converse in English. The use of a translator within a phenomenological study presents fundamental difficulties. Language is a part of the identity of the person experiencing the phenomenon. Therefore, the way in which a concept or phrase is translated could change what the participant actually said, threatening trustworthiness, credibility and dependability of the study (Squires, 2009).

Two exclusion criteria were applied:

- Individuals with serious mental illness (e.g. psychosis) were excluded; referrals would come from health professionals who have access to medical notes and would therefore be able to assess this.
- Individuals incarcerated within either of the two prisons served by NHS Lothian were also excluded. The experience of being HCV positive within a correctional facility will be influenced by the very specific set of circumstances present within that unique environment, along with its associated pressures and stressors (e.g. Yap *et al*, 2014). Whilst a valuable line of enquiry, it was not within the scope of this study.

3.4.1.3 Sample size

The sample size needed to be large enough to allow for meaningful comparisons between the factors identified in the maximum variation sample, but not so large that detailed and nuanced analysis of the data would become impossible (Mason, 2002). With this in mind, a maximum sample size of 30 HCV positive individuals was decided upon. The predicted sample numbers for the maximum variation characteristics identified were based on demographic data obtained from a local HCV patient database (A. Wilson, personal communication). The rationale for this approach was not an attempt to produce a sample that was necessarily representative of the clinical population, but more a common-sense indication of how prevalent that particular characteristic was, and therefore the likelihood of capturing that variation within the maximum sample size. Initial target sample numbers, along with the actual composition of the study's participants are shown in table 3. Twenty participants in total were recruited to the study. This was considerably lower than the maximum figures suggested, principally due to the difficulty in recruiting individuals who did not engage with HCV specialist care.

3.4.1.4 A note on saturation

The concept of saturation is often cited as a guiding principle of sample size during qualitative data collection and analysis (Mason, 2010). Two types of saturation are

commonly discussed: data saturation and theoretical saturation. Both of these concepts involve continual sampling until either no new information is obtained, or no new themes are identified (Walker, 2012). The point at which saturation is achieved can be an elastic notion (Mason, 2010), and the whole concept has been described as vague and lacking definite rules. Indeed, many authors state saturation has been achieved but fail to provide any evidence as to how it occurred (Bowen, 2008).

Table 3: Target recruitment numbers and actual number of participants obtained within the maximum variation sample, plus additional socioeconomic demographic data.

| Maximum Variation Characteristic | Variable | Maximum Target Number (n=30) | Actual Number Obtained (n=20) |
|--|-----------------------|---------------------------------|----------------------------------|
| Engagement with specialist HCV care | Engaged | 20 | 18 |
| | Not engaged | 10 | 2 |
| Date of HCV diagnosis | Pre-2011 | 15 | 12 |
| | 2011 and after | 15 | 8 |
| Mode of acquisition | Injecting drug use | 22 | 13 |
| | Other | 8 | 7 |
| HCV treatment history | Previous treatment | 8 | 3 |
| | No previous treatment | 22 | 17 |
| Gender | Male | 18 | 11 |
| | Female | 12 | 9 |
| Ethnicity | White British | 27 | 18 |
| | Other | 3 | 2 |
| Degree of liver disease | Pre-cirrhotic | 20 | 13 |
| | Cirrhotic | 10 | 5 |
| | Unknown | - | 2 |
| Employment status | Paid employment | - | 6 |
| | Unemployed | - | 13 |
| | Retired | - | 1 |
| Living arrangements | Living alone | - | 8 |
| | Lives with family | - | 12 |

The concept of saturation is rooted within grounded theory, and is indelibly linked to other grounded theory concepts such as theoretical sampling and the constant comparative method (Bowen, 2008). Whilst saturation has been used within a variety of studies claiming differing theoretical perspectives (Walker, 2012), there are a

number of reasons why I have not referred to it within my previous discussion of sample size selection. A phenomenological study is fundamentally interested in subjective lived experience, and my critical realist ontological/epistemological union accepts that individuals will construct multiple equally valid perspectives on reality (Maxwell, 2012). New data will therefore always add something new, as these perspectives are theoretically infinite in number and the point at which saturation occurs within a phenomenological study would therefore be arbitrary at best. A further consideration is the requirement of NHS research ethics committees (RECs) and NHS Research and Development departments to have full details of predicted sample numbers along with a clear rationale prior to granting approval for a study's inception. The concept of saturation does not help in meeting these demands as it provides no guidance on estimating sample size prior to data collection.

Whilst a convincing concept saturation has a number of practical weaknesses (Green and Thorogood, 2014) in addition to difficulties being aligned with a phenomenological perspective. Any claims to achieving saturation within this study would therefore be precarious and may potentially affect the credibility and rigour of the endeavour. That said, whilst not claiming saturation would be achieved, it is clearly the intent of this study to describe and explore the phenomenon under investigation as fully as possible. The sample numbers, and actual number of participants recruited in this study sit within many commonly suggested ranges for an ideal sample size to achieve saturation. However, as Mason (2010) notes, whilst these suggested ranges are offered, the authors rarely present empirical arguments as to why these numbers have been settled on.

3.4.2 Data generation: interviews

Patton (2002, p.340) notes that *"we interview people to find out from them those things we cannot directly observe."* By doing so, he highlights that interviewing is not necessarily better or more desirable than other methods of data collection, but that interviewing allows access to participants' feelings, thoughts and the meanings they attach to their experience of the world: things which are not readily observable. This rather simplistic account of qualitative interviewing positions the researcher as an impassive earpiece, neutrally 'collecting' data from participants. A research interview

does not merely 'collect' data, but instead generates accounts of lived experience and its meaning through an exchange of views and dialogue between the participant and the researcher (Kvale, 2007). The data is collaboratively produced within the relational context of the interview, with the researcher helping the participants to reach beyond the superficial layers of their experience in order to generate rich, novel and informative insights (Schultze and Avital, 2011). A social phenomenological perspective demands an emphasis on understanding the participant's experience of the world from their own situation, and then interpreting how that understanding is inter-subjectively constructed (Wilson, 2002). In-depth interviews therefore offered an appropriate and compelling method to generate data which permitted such insights and reflections, allowing participants to reconstruct verbally their understandings of a phenomenon (Mason, 2002). Conducting interviews face-to-face as opposed to over the telephone or via email also allowed the establishment of rapport, an important consideration when discussing sensitive topics such as HCV and drug use (Nichter, Quintero, Nichter, Mock and Shakib, 2004).

The 20 participants undertook their initial interviews between June 2015 and December 2015. All the interviews were audio-recorded on an encrypted recording device, and then uploaded onto a secure area of the NHS server. Once this was complete, the original file was deleted from the recording device. Interviews lasted between 19 – 67 minutes with a mean duration of 39 minutes.

3.4.2.1 Semi-structured interviews

The types of interview used within qualitative research can range from the most open-ended informal conversational interview with few pre-determined questions, to a more standardized affair with the same open-ended questions being asked, in the same way and order to each participant (Patton, 2015). This study utilised a semi-structured interview approach, which sits between these two extremes. The semi-structured aspect refers to the capacity of the interview to elicit data on perspectives of salience to participants, rather than the researcher entirely dictating the course of conversation (Barbour, 2014). It aims to balance the need for the researcher's overarching agenda to be addressed, whilst allowing how the interviewee frames and understands events to be given primary importance (Bryman, 2012). In doing so, the

semi-structured interview is a valuable social phenomenological tool. It inherently accepts that different individuals experience different versions of reality, and gives scope for their version of reality to be co-constructed and expressed within the loose confines of the general topic area, and the relational context of the research interview.

The topic areas covered within the interviews were guided by an interview schedule (appendix C). The interview schedule detailed specific questions, probes and prompts within each broad topic area to help guide the conversation, and scheduled a logical sequence for these topic areas to be approached. However, the interviews were conducted with openness to changes in this sequence and the wording of prepared questions in response to specific stories or answers given (Kvale, 2007). This encapsulates a phenomenological interest in the lifeworld of the individual. Whilst a priori assumptions about human nature naturally inform the interview schedule, understanding how HCV is experienced from the point of view of the participant, in their own words, and in their own way, was of primary importance.

3.4.2.2 Piloting

The interview schedule was initially piloted with the first couple of participants to ensure it functioned well and was adept at generating the kind of information sought. This process helped to identify any questions which made respondents feel uncomfortable, or seemed not to be understood (Bryman, 2012). The pilot interviews also provided experience of using the schedule and of qualitative interviewing generally. Although I had considerable previous clinical experience of conversing with patients during consultations, in-depth qualitative interviewing is a different art which requires practice and training (Kvale, 2007). Piloting therefore provided me with more confidence, allowing early mistakes to be identified and a more accomplished interviewing style to be developed (Silverman, 2013). For example, in early interviews the question *“how has life been since your diagnosis?”* produced fairly abrupt and bemused responses, yet a minor rewording to *“tell me about your life since diagnosis”* elicited a much richer reaction. The anonymised transcripts of pilot interviews were reviewed with the academic supervisory team, and were included within the analysis.

3.4.2.3 Consideration of other data collection methods

Other data collection methods were considered for this study but were deemed unsuitable on ethical and pragmatic grounds. Focus groups could potentially have been used, although it was felt the personal nature of the topic being discussed may have resulted in a reluctance of some participants to share their experience. Other commonly cited disadvantages of focus groups also proved pertinent, such as the difficulty of assembly, the risk of dominant individuals influencing group dynamics and the risks of potential compromise to participant anonymity (Then, Rankin and Ali, 2014). Participant observation or an ethnographic approach could possibly have been employed, however practical considerations such as exactly what, who and when to observe in order to understand the experience of being HCV positive were particularly perplexing. The impact of HCV on day-to-day life could be quite episodic, which does not lend itself well to participant observation. Also, the reconstruction of life events (such as HCV diagnosis) or a focus on the future cannot be accomplished through participant observation alone (Bryman, 2012). Ethnographic approaches can also become very intrusive in participant's lives, and overcoming multiple ethical issues such as researcher safety and obtaining informed consent could have proved insurmountable given the population being studied.

3.4.3 A longitudinal aspect

For those participants who undertook a period of interferon-free HCV treatment, a longitudinal aspect to the study was developed to follow up and conduct further interviews immediately after they had completed their course of therapy. The aim of these interviews was to focus specifically on their experience of treatment. Further details of the participants involved, and how these interviews were conducted has been given in chapter seven. The maximum sample size for this longitudinal aspect of the study was set at ten. This figure was based on the number of individuals treated for HCV within the main sampling site over the preceding year (A. Wilson, personal communication), and practical considerations concerning the time required for thorough and detailed analysis of the generated data. Due to the repeated revision of national and local recommendations for the treatment of HCV with DAAs during the planning of the study (HIS and NHS National Services Scotland, 2015a; HIS and NHS National Services Scotland, 2015b), it was initially unclear how many of the proposed

sample may be eligible for interferon-free therapies. However, once recruitment and data collection began, eight of the participants were able to access interferon-free treatment and were successfully followed up.

Further interviews with this sub-group of participants were planned once they had received the results of their treatment course, focused on their experience of being successfully cured of HCV (or not). The scheduling of this final cluster of interviews aimed to provide sufficient time for the participants to acclimate the treatment result into their lives. Therefore at least three months following the news of their treatment outcome needed to have passed. As recruitment progressed, it became clear that this final stage of data generation was too ambitious. The quantity of data generated during the previous two rounds of interviews was not insignificant, and I began to doubt my ability, as a single novice researcher, to handle additional material in a meaningful way. Also, by their very nature, these interviews needed to be conducted towards the end of the three-year period available to this study, leaving insufficient time for an immersive, thorough and rigorous analysis. Whilst three interviews were conducted with participants approximately six months after their treatment had ended, the data generated within these encounters has not been included within this thesis.

3.4.4 Recruitment process

Details of sampling strategy and the rationale for the use of interviews do not address the practicalities of how potential participants would be located and approached. Recruitment to the study focused on three participant identification sites within NHS Lothian, which were identified to maximise the potential exposure to individuals who fitted the inclusion/exclusion criteria and maximum variation sampling matrix. These sites were also all locations which fostered and encouraged a culture of research, and which I had experience of working in to a greater or lesser extent in my role as an HCV nurse specialist. It was hoped that these factors would help in the negotiation of my access to the sites, but they also raised ethical issues which will be discussed further in due course.

The first recruitment site was an infectious diseases outpatient clinic based within a university hospital. This site was one of two hospital-based clinics providing specialist care and treatment to HCV positive individuals in Edinburgh. The second site was an inner city GP practice serving one of the most deprived areas of Scotland (Scottish Government, 2016). The practice had a long tradition of engaging in research, with many of the medical staff maintaining special interests in areas related to social deprivation, such as blood-borne viruses and drug use. The third recruitment site comprised a network of 'recovery hubs' situated around Edinburgh. These hubs provided a range of drug and alcohol treatment and support services on a 'drop-in' basis, run by a collaboration of NHS, social work and voluntary sector staff.

The initial approach to potential participants in all sites was via the healthcare staff who worked in each of these locations. A participant information sheet was provided for staff to give to eligible candidates when they attended routine appointment or walk-in clinics (appendix D), and if interest was shown, verbal consent obtained to pass on their contact details to me so I could phone to discuss the study in more detail and arrange to meet. It was suggested that this meeting occur when they next expected to be at the recruitment site, in order to avoid creating additional appointments, unless the potential participant wished to meet at a different time/place. At this meeting, I discussed the participant information sheet and consent form, answered all questions, and obtained written informed consent. Arrangements were then made to perform the research interview at a time/place convenient for the participant.

Following the research interview, the participant was asked if they would be happy to speak with me again, should they commence a course of HCV treatment. I explained that I would like to conduct two further interviews, one at the end of treatment, and one approximately six months after that. If the participant agreed, I obtained consent to liaise with the HCV treatment team to monitor the participant's progress through treatment, and contact them again when an end date for their period of therapy was known. Arrangements would then be made to conduct the second research interview at a time/place convenient for the participant, but as close to the end of their HCV treatment course as possible. Following the second interview, a provisional date for the third interview would be arranged for six months hence. I would contact the

participant nearer the time to confirm details and finalise plans for the final research interview.

3.4.4.1 Payment for participation

All participants were offered reimbursement for any out-of-pocket expenses incurred as a result of taking part in the study, in line with good practice recommendations for members of the public involved in NHS, public health and social care research (INVOLVE, 2010). Expenses payments have been shown to be a significant motivator in research involving PWID (Fry and Dwyer, 2001), and are associated with increased follow-up rates (Festinger *et al*, 2005) which was an important consideration given that the study contained a longitudinal element. In view of the ethical issues surrounding the award of cash payments to potentially substance-using participants, and difficulties in administering a cash payment through the hospital finance system without disclosing their identity, a £15 supermarket gift voucher was offered for each interview attended. Whilst this voucher was gratefully received by most participants, three individuals expressed discomfort at what they perceived as payment for their participation in a study they had voluntarily signed up for.

3.4.5 Data management and analysis

3.4.5.1 Transcription

Verbatim transcriptions of the recorded interviews were made using *Olympus AS-7000* transcription software and stored in a secure area of the NHS server. Patton (2015) suggests that completing your own transcription offers an opportunity to become immersed in the data, an experience which can help with the generation of emergent insights. Indeed, Ryan and Bernard (2003) note that the process of analysis probably begins with the transcription of audio recordings. For these reasons, I transcribed all the interviews myself. During this process, the data was anonymised by giving each participant a pseudonym (which they were invited to choose), and changing any other potentially identifiable information such as the names of friends and family, locations, dates, name and titles of professionals etc. Once anonymised, the transcripts were checked to ensure they were non-identifiable by a member of the supervisory team.

3.4.5.2 Thematic analysis

Thematic analysis is a method for identifying and analysing patterns of meaning (themes) within a data set, and illustrating the importance of those identified themes to the phenomenon under investigation (Braun and Clarke, 2006; Fereday and Muir-Cochrane, 2006). It is not tied to a particular theoretical framework, and can be applied across a range of epistemological positions (Joffe, 2011) being a method which can equally illuminate realist and constructivist paradigms, both reflecting reality and unpicking and unravelling the surface of 'reality' (Braun and Clarke, 2006). Thematic analysis has only relatively recently been acknowledged as a qualitative analytical method in its own right, having previously been regarded more as a component of other 'branded' forms of analysis such as interpretive phenomenological analysis (IPA), discourse analysis or grounded theory (Braun and Clarke, 2006; Bryman, 2012; Joffe, 2011). Whilst the identification and analysis of themes is indeed a necessary generic skill and unifying principle for much qualitative research, thematic analysis as a defined qualitative method strives to do this in a systematic and transparent way, upholding the importance of the pervasiveness of themes without sacrificing depth of analysis (Joffe, 2011).

The lack of explicit recognition thematic analysis historically invited masks the disparity between its perception as being unsophisticated and indistinctive, and its wide, though frequently unacknowledged use in qualitative research. Braun and Clarke (2006) argue that because thematic analysis is poorly demarcated and defined, analysis that is often claimed as following other methods, or more often not identified as a particular method at all (e.g. 'data subjected to qualitative analysis for recurring themes') is in actuality, thematic analysis. By clearly appropriating and naming thematic analysis as the analytical technique employed in this research, I seek to avoid 'method-slurring' (the blurring of distinctions between various theoretical perspectives and methodological techniques [Baker, Wuest and Stern, 1992]), and to improve clarity, consistency and coherence, whilst contributing to the overall integrity and rigour of the study (Holloway and Todres, 2003). As a hallmark of thematic analysis is its theoretical flexibility, it is necessary to discuss the appropriateness of its adoption within the social phenomenological framework of this research.

3.4.5.3 Social phenomenology and thematic analysis

The approach to data analysis employed within any research project should be driven by its appropriateness to the research questions and the theoretical perspective underpinning the investigation, rather than by staunch 'methodolatry' (Holloway and Todres, 2003). Joffe (2011) notes that thematic analysis lends itself well to a critical realist social phenomenological perspective, and examples of previous research employing this union are found within health and social science. These examples include studies where thematic analysis has been explicitly stated as the data analytical tool (e.g. Carroll, Rothe and Ozegovic, 2013; Fereday and Muir-Cochrane, 2006), and also where thematic analysis is not specifically asserted but its methods are described (e.g. Carvalho, Merighi and Jesus, 2010; Ferreira-Umpiérrez, 2013; McWilliam *et al*, 2009).

Thematic analysis can capture the divergence and subjectivity of individual participant responses, in addition to describing and interpreting meanings across participants, however does not share the idiographic focus of a methodology such as IPA (Braun and Clarke, 2006). As previously discussed, Schütz believed that inter-subjectivity was the foundation of all human knowledge and experience, and that the way humans construct their perspective and attach meaning to the outside world is not a purely individual process (Ajiboye, 2012). He made a distinction between first- and second-order constructs within social science research. The first-order, reflecting the common-sense experience of the everyday inter-subjective world by the people being studied (McWilliam *et al*, 2009), and the second-order being the researchers own constructs and interpretations of the commonalities and meanings within those subjective experiences (Aspers, 2009):

"The thought objects constructed by the social scientist, in order to grasp this social reality, have to be founded upon the thought objects constructed by the common-sense thinking of men [sic], living their daily life within the social world. Thus, the constructs of the social sciences are, so-to-speak, constructs of the second degree, that is, constructs of the constructs made by the actors on the social scene"

(Schütz, 1962 p.59)

By describing these orders, Schütz sought to distinguish between practical (first-order) and theoretical (second-order) modes of interpretation, arguing they involve fundamentally different ways of relating to an experience (Ostrow, 1990). These second-order 'theoretical' constructs should always be founded on first-order subjective experiences, but are in effect the researcher's inter-subjective interpretations of the phenomenon's meaning. These inter-subjective interpretations are Schütz's ideal-type. That is, the commonalities (or themes) among people's subjective experiences, or the essence of a phenomenon. With this in mind, thematic analysis within this theoretical framework offers a compelling fit, as it allows the exploration, description, construction and interpretation of these commonalities of experience, using an analytical approach which recognises themes across an entire data set rather than focusing meticulously on the individual.

3.4.5.4 Identifying themes

The identification of themes within the data set can be one of the most mysterious tasks in qualitative analysis (Ryan and Bernard, 2003). Indeed, it is not uncommon for research reports to describe themes 'emerging' from the data in lieu of detailed description of the actual analytic procedures undertaken (Braun and Clarke, 2006). What constitutes a 'theme' is also often poorly defined, and is not helped by the wealth of terminology used throughout the literature to describe similar analytical ideas e.g. categories, patterns, codes, labels, memos, expressions, incidents, segments, thematic units, data-bits, chunks, concepts, units etc. (Ryan and Bernard, 2003). Bryman (2012) provides some broad clarity, noting that a theme is a category identified by the analyst through their data, relating to the research focus and building on the codes identified in transcripts and/or field notes. A theme should also provide the researcher with the basis for a theoretical understanding of the data (Bryman, 2012). For clarity, the analytical process which led to the identification of the three over-riding themes from the main body of data (chapters four to six), and the three themes related to the experience of interferon-free HCV treatment (chapter seven) will now be detailed.

The six phases of thematic analysis described by Braun and Clarke (2006) formed the basis of the analytical approach. The first phase involved familiarisation with the

complete data set, which was achieved through the transcription of interviews and repeated reading of the resulting transcripts. During this immersion in the data, a research diary which had been kept throughout the planning and implementation stage of the study was used to take initial notes, and record features of the data which seemed significant or interesting. The second phase involved coding the transcripts, which contained both deductive and inductive elements. A broad coding framework was initially devised, informed by categories found in previous qualitative research concerning the lived experience of HCV (see chapter two). It was considered reasonable to assume that wide-ranging categories derived from previous studies would remain a feature of living with HCV, despite the witnessed advances in treatment. For example, 'stigma' and 'symptoms' formed two of the initial deductive codes, which were then augmented by more detailed inductive codes formed from initial impressions of the corpus of data. This approach served to assist with the early analysis of the data, but inductive codes were also developed as novel and unexpected insights were met. The transcripts of the initial interviews with all 20 participants were coded in this manner.

The transcripts of the second interviews with the eight participants who undertook a period of interferon-free treatment were handled in a similar way. Again, a broad framework of deductive codes was devised based on previous qualitative research focused on interferon-based therapy. It was deemed reasonable to assume that expansive categories such as 'side-effects' and 'support' would transcend the specifics of the medications involved. Inductive codes formed from readings of the data set were added to this basic structure, and then further enriched as coding of the transcripts progressed. Treatment related codes from the initial interviews of these eight participants were included within this branch of analysis to allow for the comparison of pre- and post-treatment narratives.

In both branches of analysis, the deductive and inductive codes were then combined, reviewed and revised, a process which drew groups of codes together to form a number of sub-themes (phase three). Whilst depicted as a linear progression, the interviewing, transcribing and coding process occurred in parallel, with each activity informing the others. Phase four of analysis drew the sub-themes together, combining

them into candidate themes which were examined in relation to the corpus of data, field notes, and the research diary. During this process, I met regularly with three academic supervisors to review, challenge and interrogate the evolving analysis. The fifth and sixth phases of analysis entailed defining the candidate themes, and writing-up the findings in a concise, coherent and logical manner. NVivo v.10 software was utilised during the thematic analytical process. All anonymised transcripts were uploaded within this application, which aided the organisation, coding and retrieval of data.

The iterative approach to research continued throughout all six phases of analysis. For example, coded fragments of data which had been drawn together into sub-themes were recurrently re-examined within their original narrative flow to ensure their meaning had not been decontextualised. During the writing process, interpretations of candidate themes were interrogated in relation to the raw data found within the transcripts, grounding the analysis in the subjective life-worlds of the participants and ensuring the findings remained recognisable and familiar. This iterative approach to research aimed to address Schütz's postulates of subjective interpretation and adequacy (section 3.3.4.2), which state that constructions of human action must be grounded in the subjective meaning the 'actor' had for the action, and be recognisable and understood *by* that actor (Schütz, 1973).

3.4.5.5 Trustworthiness and rigour

The trustworthiness and rigour of this endeavour were further enhanced in a number of ways. Regular meetings with the academic supervisors to this project helped to contest and question the analysis as it progressed, aiding the suspension of belief in the existence of the world as I know it. Immersion in the full dataset by one of the supervisors helped to ensure the findings remained data-driven and rooted in the narratives, rather than becoming too removed from the participants' voice. Also, nonconforming cases were identified during the analysis and presented as part of the findings, providing, where available, an alternative and legitimate perspective on the lived experience of HCV and its treatment.

3.4.6 Ethical considerations

Ethical issues relate directly to the integrity of a piece of research, and discussion of ethical issues forms a central focus when planning research and obtaining approvals from funding bodies, professional associations and recruitment sites (Bryman, 2012). During the planning of this study I intuitively engaged in constant reflection of the ethical issues involved, although the process became more formalised whilst preparing my submission to the NHS REC. The ethical issues discussed here are therefore those which primarily relate to the relationship between the research participants and myself, which were the main focus of that submission. They include recruitment, informed consent, potential risks of harm to participants, handling sensitive topics and the disclosure of sensitive personal information, and my own personal safety in conducting fieldwork.

3.4.6.1 Recruitment

As I had previously worked as an HCV nurse specialist, there was a possibility that I would be known to some of the potential participants. To avoid influencing individual decisions as to whether to take part, I did not approach potential participants directly, until they had been introduced to the study by their regular healthcare professional and shown interest in participating. If a participant showed any recognition towards me, or asked about my background I was upfront and honest regarding my previous role, but made it clear that I was currently working as a researcher and was not part of the clinical team.

3.4.6.2 Informed consent

The principle of informed consent is enshrined in research practice, and mandates that prospective research participants should be given as much information as they require in order to make an informed decision about whether or not they wish to participate in the study (Bryman, 2012). However, this presents informed consent as a one-off procedure, attended to during the recruitment of participants and never thereafter revisited (Barbour, 2014). In reality, informed consent presented a number of ethical issues within this study in addition to ensuring potential participants had sufficient information. For example, as previously discussed I was aware that a requirement of the NHS REC was that I did not approach potential participants myself to avoid any

intended or unintended coercive influence. However, it is also important to acknowledge the latent persuasive influences other people may exert (Mason, 2002). For example, HCV positive individuals were initially approached by their regular healthcare workers which could result in individuals agreeing to participate, and giving 'informed' consent, out of a wish to please their care providers and not appear 'difficult'. Or conversely, the healthcare worker could exert inadvertent and subliminal pressure on the individual to agree to participate out of friendship or loyalty to me, or a wish for my study to succeed.

The discussion of giving potential participants sufficient information to make an informed decision is also interesting, as it is extremely difficult to present prospective participants with absolutely all the information that might be required (Bryman, 2012). For example, one of the main research questions within this study focuses on whether HCV positive individuals view their infection as a chronic condition. This information was not disclosed to the potential participants due to concerns about contaminating their answers. This meant that although the goal of understanding what it is like to live with HCV was clearly stated, the reasons why I wanted to know this were consciously omitted. As a result, participants agreed to be interviewed about living with HCV, but ultimately were not aware of what questions or aspects of their lives I would be focussing on. Mason (2002) highlights this when she advises that giving informed consent to be interviewed, is not consenting to answer anything the interviewer may ask. For this reason, informed consent was revisited throughout the interview: checking participants were OK to carry on during difficult topics; offering to move to other subjects; or suggesting the interviewee take a break.

The issue of capacity to give informed consent was also an important consideration within this study given participants may present with comorbid substance use. The condition of being dependent on a drug does not in itself preclude capacity to give informed consent, but it may impair that capacity by affecting an individual's ability to weigh up information, make free and informed decisions and exercise autonomy e.g. if they were in an extreme state of intoxication (Smith, 2008). Capacity is also not absolute, and could fluctuate between the point of obtaining consent and conducting the interview, or possibly within the timeframe of an interview itself. For these

reasons the decision about whether an individual had the capacity to give informed consent was taken on a case-by-case basis, and constantly monitored throughout the subsequent interview. If an individual was deemed too intoxicated to make an informed decision, which occurred on one occasion, the interview was rearranged for another time.

3.4.6.3 Risks of harm to participants

Harm comes in many guises, and good ethical practice encourages researchers to anticipate and guard against any harmful consequences which can be predicted (Bryman, 2012). The main risk of harm identified for participants in this study was potential for emotional distress during the interview process due to the sensitive nature of some of the topic areas being discussed. Patton (2015) notes that qualitative methods are highly personal and highly *inter*-personal, and because in-depth interviews are designed to open up and probe participants' experiences of a phenomenon they may be more intrusive and involve greater reactivity than quantitative methods. It was therefore necessary to incorporate the potential for this into my interview style, approaching sensitive topics carefully and thoughtfully, pre-emptively reassuring the participant that they would receive an empathetic and considerate response should they become upset and wish to stop. It was also important not to simply 'take the data and run' (Barbour, 2014), and an emphasis on how the interview was drawn to a close and the importance of debriefing were vital. Thompkins, Sheard and Neale (2008) discuss the benefits of ending interviews with female PWID by focusing on more positive topics, concentrating on plans and hopes for the future. This strategy was employed within this study, in addition to utilising a debrief sheet containing contact details for a number of local support groups and charities. However, only one participant took the debrief sheet away after the interview, although it was offered to all participants.

Within the interviews, it was also likely that criminal activity in relation to drug taking would be disclosed, in line with the level of disclosure found in routine clinical practice. It was considered unlikely that a participant would disclose anything more serious, but in order to mitigate risk to my own legal position and the need to break confidentiality, I advised interviewees not to disclose information regarding serious offending for

which they had not been convicted (Orb, Eisenhauer and Wynaden, 2000). They were also advised that I may need to speak to others should they discuss anything which indicated harm to themselves or others in line with NHS Lothian child and adult protection procedures.

3.4.6.4. Confidentiality

The issue of maintaining a participant's confidentiality stems from the same ethical principle as minimising the risk of harm (Bryman, 2012). Confidentiality and anonymity are often used as analogous terms within qualitative research, and within this study all participants were assigned a pseudonym and patient identifier number during the process of taking informed consent. Further, during the process of transcription, any other identifiable information such as the names of family and friends, specific locations, number and gender of children etc. were also changed. Barbour (2014) notes, however, that names are only one among many details which can lead to individuals being identified, and it can be difficult to anticipate which aspects of the descriptions might give rise to an individual being recognised. This line of thought was pursued by the NHS Caldicott Guardian during the study's approval process, which had implications for data storage, data management and subsequent analysis. To ensure the anonymised transcripts were sufficiently non-identifiable, they were initially sent via secure nhs.net email to Dr Anne Whittaker, a supervisor of this study who also has an NHS contract of employment. Only once they had been assessed in this manner (and necessary alterations made where appropriate), were the transcripts moved from the secure NHS server and analysed through NVivo software available at Edinburgh Napier University.

Whilst protecting the privacy of research participants is a dominant ethical principle, there are reports of participants who wish to be identified and recognised for the contributions they have made (e.g. Patton, 2015; Silverman, 2013). A number of participants in this study also voiced their desire to be visible within the final report. This highlights an interesting debate; in our rightful quest for ethical practice, are we removing the right of participants to make free and informed decisions about how their data is used?

3.4.6.5 Researcher safety

The safety of researchers during data collection is an important ethical consideration, but one which is often overlooked (Barbour, 2014). As I would be working alone and conducting interviews in various locations, including participants' homes, safeguards were put in place to address this. Where interviews took place in one of the recruitment sites, I notified reception staff when entering the interview room and advised how long the interview was expected to last. I also employed personal security devices in places where these were routinely used by staff. In locations where reception staff were unavailable, the NHS Lothian lone working policy was adhered to.

3.4.7 Summary

This chapter has aimed to provide a comprehensive overview of the methodology which underpins this study, and the practical methods employed in the generation and analysis of data. It has illustrated how the theoretical perspective of social phenomenology has guided applied research practice, and addressed the ethical considerations which such applied research methods demand. The following four chapters present the outcome of this process: the study's findings. Chapters four to six each focus on one of the three major themes which resulted from the analysis of the data, describing the contemporary lived experience of HCV. Chapter seven sits apart from the main body of results, and examines the three additional themes which collectively explore the lived experience of interferon-free treatment. The final chapter, chapter eight, considers these themes together, and discusses them in light of the research questions. Implications for policy, service delivery and clinical practice are then examined, along with the limitations of this piece of work.

Chapter 4

Positioning hepatitis C

4.1 Introduction

Analysis of the data generated during the participant interviews resulted in three predominant themes which capture the central common features of the participants' subjective experiences, exemplifying Schütz's 'ideal type'. The explication of these principal themes over the next three chapters aims to describe and interpret the inter-subjective understandings in light of existing knowledge and associated theories, whilst also illustrating how the social reality portrayed remains grounded in the subjective point of view of the participants (Schütz, 1973). The themes have been named 'positioning hepatitis C', 'beyond a physical burden', and 'reconstructing uncertainty'. The titles of these overarching themes seek both to capture the internal homogeneity of the data collected therein, and to highlight the external heterogeneity between them (Patton, 2015), whilst giving a practical sense of the analytical thrust each theme contains (Braun and Clarke, 2006).

The theme 'positioning hepatitis C' proved resilient and robust during data analysis. It illustrates how the experience of being HCV positive was not understood in isolation by the participants, but positioned within wider sociocultural, medical and politico-economic contexts. It describes how the lived experience of HCV was negotiated and renegotiated over time in relation to multiple factors, rather than being an invariant and static reality. Comparisons and assessments were commonplace within the participants' narratives, contrasting and evaluating their own experience of being HCV positive in light of the circumstances of their daily lives, others they knew, and broader external influences. 'Positioning hepatitis C' aims to emphasise the contingent nature of the lived experience, by exploring how understandings of the disease were comparative and positional.

The descriptions of diagnoses which begin this chapter establish this theme well. Participants' situated the disease within the sociocultural context of their lives at the time, which resonates with earlier work in this area. However, the theme goes further

and expands on these familiar reactions, to illustrate how understandings of the disease itself became fractured as contextual comparisons were drawn to other people living with HCV, the condition of their liver, and the inequalities of access to treatment. This chapter aims to illuminate how the lived experience of hepatitis C was dynamic and relative, describing how participants positioned the disease in relation to multiple internal and external factors.

4.2 Diagnosis

4.2.1 Starting points

I started each of the pre-treatment interviews by asking the participants to tell me about their diagnosis²³. This was a conscious decision, designed to allow the participant to ease into conversation by speaking about a verifiable situation, prior to being asked more conceptual questions related to their thoughts, feelings and understandings (Kvale, 2007). However, it also immediately designated and labelled the participants as members of a particular category - that of someone with HCV - and subsequent descriptions of their experiences of diagnoses were therefore imbued with specific qualities (Potter, 1996). For example, whether it was good or bad, significant or trivial, unpredicted or expected, distanced or aligned them with notions of what being part of that category signified within society. Subjective meaning was embedded into objective description during these conversations, conveying a sense of self, or more accurately a cluster of traits which suggested a particular persona (Harré and van Langenhove, 1999a). This served to make ensuing discussion of their version of reality seem more credible and dependable (Potter, 1996). These diagnostic stories were generated within the context of a qualitative research interview, and should be treated as selective and potentially strategic (Barbour, 2014). That is not to say they are apocryphal, merely that the participants were producing an account of their diagnosis and offering a narrative and persona that was purposeful and deliberate to the circumstances they were in.

These purposeful narratives of diagnosis offer a pathway into the data, and provide a natural starting point for the examination of participants' experiences of HCV.

²³ "I'd like to start by talking about when you were diagnosed. Can you tell me what happened?"

Diagnosis is integral to the system of medicine and the way it creates social order (Jutel, 2009), and for social scientists the process of making that diagnosis is central to subsequent constructions of the illness (Brown, 1995). Diagnosis embodies the time and place when permission is given to be 'ill', when medical professionals confer legitimacy on a condition and begin to offer an explanatory framework. As Jutel and Nettleton (2011) note, diagnosis is a starting point; the foundation from which sense-making and experience are crafted.

The starting points for the participants in this study were many and varied. Diagnoses were received following routine GP appointments, antenatal checks and following blood donation. A number of participants were diagnosed whilst hospitalised with other conditions, primarily drug related, or tested and notified whilst in the process of accessing opioid substitution therapies. Not all diagnoses were made in traditional healthcare settings however. Prison, a health food shop, and a private detoxification clinic also featured in the collected narratives, which covered a period of 24 years from 1991 to 2015. For two participants, the diagnosis of HCV was received on more than one occasion due to reinfection, one following successful treatment and the other after spontaneous clearance of the virus. The following analysis seeks to describe and interpret the participants' accounts of their diagnosis experience, positioning it within their lives at the time and providing a foundation for subsequent discussion of how these understandings of HCV were modified and revised as participants lived with the virus and came to understand it from a new standpoint.

4.2.2 A contextual diagnosis: drug use

The participants described a reaction to their medical diagnosis of HCV which positioned it within the sociocultural context of their lives at the time, and echoed the findings of earlier work in this area (e.g. Olsen *et al*, 2012). For those who had no history of drug use, or who had moved on from a drug using past, feelings of shock, anger, denial and depression were widespread, with fears and concerns for an indefinite future and disbelief that this could happen to them writ large within their narratives. The impact of the diagnosis was often explicitly stated and emphasised with the use of metaphor and idiom:

...it was more, more it jus' hit me like a tonne a' bricks when he jus' walked in an' said it an' walked out, y'know. I didn't get an explanation or anything...

(Jacqueline, 70, diagnosed 1991)

So I'd made appointments, made a lot of, few appointments wi' my own doctor, taken blood samples, an' then got a letter through the door that said she would like to speak to me, an' then she jus' dropped a bombshell on me. An' that's when I found out...

(Stewart, 52, diagnosed 2015)

For those participants who situated their medical diagnosis of HCV within a period of drug use, a less traumatic reaction to the news was portrayed. Although participants recounted feeling foolish, upset and angry, these feelings were played down within the narratives as participants sought to produce a socially acceptable account of their response at the time. The participants portrayed their anguish at being diagnosed with HCV as mitigated by a view that their own behaviour was primarily to blame for the infection, and a perception that they had put themselves at risk. The distress felt at the diagnosis was depicted as tempered by their sociocultural environment at the time, and a life revolving around a frenzied addiction. Descriptions of life around the time of diagnosis vividly related accounts of unsafe injecting practice, overdose and “*constantly chasing your next fix*”²⁴. Ultimately, the medical diagnosis of HCV was portrayed as foreseeable and almost predetermined, demonstrated by the lack of surprise that suffused these narratives:

I: So when you found out, how did you feel?

K: [pause] Gutted. But, it was, it wasn't a big shock, because I knew I had been really un-careful an', 'cause I was in the madness an' stuff I jus' wasn't really caring about mysel' an' was jus' sharing wi' loads a' people eh an' [draws in breath], so, no, I was gutted but it wasn't a big surprise.

(Kelly, 34, diagnosed 2008)

...but aye, it was, it was pretty devastating, but the same time I sort a' had that attitude well ken what, you knew what you were doing at the time, you knew the risks you were taking, things we do a' get stoned eh?

(Eilidh, 39, diagnosed 2013)

²⁴ Paul, 37, diagnosed 2000

For these individuals, a process of social diagnosis had begun prior to being medically labelled as HCV positive. A social diagnosis considers not the presence or absence of a particular virus or bacterium, but the larger political, economic, cultural and social structures which contribute to making that diagnosis (Brown, Lyson and Jenkins, 2011). By identifying as a person who injects drugs, the narratives generated here reveal a socially-produced diagnosis of 'pre-HCV', which explicitly considers the potentiality of this future condition. The presence of such a social diagnosis constrained the way these individuals were able to talk about their reaction to the subsequent medical categorisation, producing accounts which positioned a diagnosis of HCV as inexorable and normalised. These accounts reduced the primacy and authority of HCV, and reinforced prevailing societal attitudes to drug use and PWID. The way in which HCV was characterised as a disease of addiction was reflected in the discourse that PWID themselves used to position HCV within the context of their own lives:

I didn't really take a lot of notice of it, to be honest. Err, if I'm honest about it, looking back on it now, in hindsight (...). To me, it was jus' another, oh, you've got this, or you've got that, or whatever, y'know, who cares like?

(Phil, 60, diagnosed 1997)

This insight resonates with the work of Davis and Rhodes (2004), whose interviews with PWID in London depicted HCV as a ubiquitous risk, and an almost inevitable consequence of a drug using lifestyle. Drug use and HCV become conflated into one expected life trajectory, where the eventual medical diagnosis of HCV was portrayed as a predictable and preordained destiny.

4.2.3 A contextual diagnosis: co-morbidities

Whilst those diagnosed within a period of drug use still reported dismay at the news, albeit moderated by the context of their lives at the time, a comorbid HIV infection appeared to almost negate such emotional reactions entirely. For these individuals, a diagnosis of a further blood borne virus was portrayed as holding little significance when placed within their experience of living with HIV. The participants produced accounts which emphasised a keen sense of apathy and disinterest:

I was actually, no' numb or anything, jus' indifferent, because of my HIV status, I jus' thought oh that's another disease I've got, an' even when I got told it was genotype one which is the best-yun [laughs ironically], sorry – err, I mean I dunnae go for things by half eh? But err aye, I jus' thought it's another, disease; 'cause, I always assumed that HIV was gonna kill me anyway.

(Keith, 54, diagnosed 2004)

I: Did anything change for you when you were diagnosed hep C?

C: No, I just, I just took it, I was hepatitis B, and then "oh, alright", an' then, I dun' ken what year I was hep C, an' it wasn't a big deal to me, y'know what I mean?

(Callum, 52, diagnosed approx. 1995)

I actually erm, I sometimes forget that I've got hep C, it's just away back there somewhere [indicates back of her head] and err, I think "Oh yeah, I've got that as well"

(Sheila, 59, diagnosed 1991)

Accounts of a diagnosis of HCV being over-shadowed by an existing HIV infection also echoed previous studies, where HCV was often framed as less significant in terms of its gravity when considered alongside the more knowable and definite HIV (Copeland, 2004; Davis and Rhodes, 2004). This was not the only disease comparator utilised by the participants, however, with other chronic conditions such as diabetes and various cancers also recurrently providing context. Cancer was consistently framed as a more serious and onerous diagnosis, and stories of personal experiences with cancer, or of others known to the participants were used to illustrate the perception that, despite everything, things could be much worse:

...she walk through the door, when I saw her, I went like 'Oh. My. Gosh'. She has cervical cancer, and it went downhill in a way that [pauses] you can imagine. And she just burst into tears, and say 'Oh Peter, look what's happened to me' and I thought, what's the point for me to tell her I have hepatitis C, it's nothing comparing what she's going through.

(Peter, 51, diagnosed 2015)

4.2.4 The influence of treatment

Whilst the sociocultural context of individuals' lives at the time of diagnosis shaped their reaction, the timing of that diagnosis within the context of HCV treatment evolution and advancement appeared to have little influence. Roughly equal numbers of participants were diagnosed before and after the start of the DAA era in 2011, yet narratives around response to diagnosis did not reflect any recognition of these biomedical developments. Participants diagnosed after the advent of DAAs continued to report significant emotional distress. Indeed, some of the most vivid and striking accounts of intense reactions to diagnosis came from participants who received the news most recently:

I remember going to the, the nurse, and err, my mum was with me, an' I remember they read out, y'know the hep B, hep A blah blah blah, AIDS an' all that, an' [pauses] it, we were sitting there, an' they said hep C – positive [pauses] an' [pauses] I was, I jus' [blows out air] God, blanked out, I, I, I went into shock, 'cause all I remember hearing was, my mum going "oh my God" and they ended up having to go an' get the doctor because I had went into shock...

(Anita, 46, diagnosed 2014)

Of note, Anita professed to have very limited understanding of HCV at the time of her diagnosis, and her explanation for her intense reaction centred on a half-remembered story she had read concerning a celebrity with HCV taking interferon. While the influence of interferon on the understanding of HCV will be examined in greater detail within chapters six and seven, a discourse which comprised intense distress, disbelief and depression remained critical to the participants' experiences of HCV diagnosis in the era of DAAs. Accounts of diagnosis post-2011 were indistinguishable from those who had been diagnosed further in the past, strongly resembling the stories of HCV diagnosis made during the height of the interferon era. Similar findings have been reported previously in relation to other conditions which resonate here. Flowers, Davis, Larkin, Church and Marriott (2011) focused on accounts of HIV diagnosis made to gay men in Scotland after the introduction of Highly Active Antiretroviral Therapy (HAART). They described reactions to HIV diagnosis that resembled those documented in the stages of the epidemic which preceded the advent of HAART, and cautioned that despite the 'brilliance' of effective HIV treatment, the psychological and social concerns about HIV endured, or were reshaped in light of the contemporary situation.

Similarly, in their review of the impact of HAART on the psychological distress of people living with HIV, Siegel and Lekas (2002) found no clear evidence to suggest that the availability of these drugs had lessened the impact on individuals' emotional response to infection.

4.2.5 Re-evaluation of life: alcohol

Following an HCV diagnosis, a re-evaluation of life and an attempt to regain control have previously been well described in the literature (e.g. Faye and Irurita, 2003). Illustrations of this reconsideration of priorities were manifest within this study too. For example, a diagnosis of HCV provided impetus to change the relationship with alcohol cultivated by a large number of the participants, bringing established drinking patterns and habits into question. Many of the participants described themselves as heavy drinkers or alcoholics in the past. However, the implications for their health of an excessive alcohol intake appeared to be unfamiliar, or disregarded, until an HCV diagnosis was made. This is well illustrated in the following quote. Happy recounts her thoughts on her pre-diagnosis lifestyle, juxtaposing an idea of 'health' alongside an acknowledgement of drinking to excess:

...all along, I've, I've been thinking that I was healthy, I haven't been paying much attention, and I was also drinking a lot.

(Happy, 51, non-cirrhotic)

An HCV diagnosis provided a point of re-evaluation for the participants, placing their drinking under scrutiny in the context of a perceived greater threat. For many, stopping drinking was seen as a protective action, aiding the recuperation of what was frequently assumed to be an already damaged liver, presented within the narratives as adhering to healthcare messages and 'doing the right thing' (Harris, 2010). However, eliminating alcohol was also framed as a pre-emptive assault on HCV itself, preparing and galvanising the body for a period of treatment:

I'm not jumping on the temperance bandwagon or anything like that, erm, but I would say that, cutting out alcohol ages prior to treatment is a good thing, I can't imagine if you were, y'know, erm, an alcoholic with an already y'know, erm, overloaded liver, erm, an' then you was gonna go through the treatment

[blows out cheeks] I mean it's like sort of making life as incredibly difficult for yourself...

(John, 54, non-cirrhotic)

Complete abstinence was not a uniform reaction, with some participants describing a more measured and nuanced approach to addressing their alcohol consumption, echoing previous work in the area (Stoller *et al*, 2006). The moderation of frequency, volume and type of alcohol were offered within the narratives as evidence of moral agency, but with the caveat that they permitted a variant of normal life to continue:

I'm, to this day, I'm no' totally alcohol free, I have been since the first of January, for a dry January for me, but, I'm, I'd still say that, goin' oot, or having someone round, I'll still will have a couple a' beers but I'll no' be drinking a case a' beer a night, or drinking like your vodka, or anything like that.

(Stewart, 52, cirrhotic)

Whilst these findings align with some previous studies suggesting an HCV diagnosis is associated with reduced alcohol consumption (e.g. McCusker, 2001), the published literature remains divided on the topic, with the complex interplay between HCV and alcohol consumption explored more fully by a small body of qualitative research focused on the issue. For example, in work conducted with HCV positive individuals in Australia and New Zealand, Harris (2010) described how the ubiquity and normalisation of alcohol use in Western culture, equivocal medical advice espoused by various health professionals, and a misplaced faith in ALT results presented social and psychological barriers to the renegotiation of alcohol use for individuals with HCV. Alcohol consumption was not a specific topic within the interview guide for this study, and the insights presented here are drawn solely from spontaneous discussion precipitated by the participants, possibly contributing to their uniform discourse of alcohol reduction. It is also possible that the homogeneity of the healthcare team providing care for the participants had instilled a consistent message regarding alcohol use, which was reproduced in the interview setting to present a persona of compliance to the researcher.

4.2.6 Re-evaluation of life: drugs

Transformation narratives were evident within many of the interviews, as participants described making dietary changes and actively seeking out HCV information. The diagnosis of HCV spurred a general desire to live a healthier, socially conventional and more routine lifestyle, positioning the disease as a turning point and the start of a fresh chapter in their lives. For a couple of participants who were using drugs at the time, the diagnosis also provided the impetus to engage with drug services and start to address wider concerns:

...an' then it was like, now I've got a' start taking care a' myself, I've got a' start eating better, I've got a' start trying a' maintain some sort a' routine in my life to hold my job down...

(Fiona, 40, diagnosed 2012)

I started thinking right, obviously certain things in my life were gonna have to change, it, it focused me as well and it pushed me to just get rid of the heroin and get that out the way an', an' an' jus' move on with getting onto the Subutex.

(Gary, 38, diagnosed 2013)

It wasn't all such optimistic news, however, as a re-evaluation of life did not always equate with an attempt to regain control. A more common reaction to being diagnosed with HCV amongst those who were using drugs at the time was a descent into ever greater drug use associated with feelings of hopelessness, and that there was now nothing to lose:

but, I think that sort a' made my drug habit out a' control when I found out I had hep C very out a' control, I jus' felt that, now I had that, I didn't have anything else to live for after that, erm, so, all I done was took more an' more drugs, constantly, for all they years...

(Danielle, 43, diagnosed 2009)

S: *...when you think you've got a fatal illness 'cause of what you're doing in your life (...) it's always in the back of your mind like, y'know, an' you jus' get that don't care attitude - don't care, don't care, don't care, don't care - so you use more, do more - don't care, don't care - go to prison - don't care - stick me in a psychiatric ward - don't care - y'know, jus' don't care. Y'know, err...*

I: *Because you think...*

S: *Yeah, because you think you're dying.*

(Steve, 45, diagnosed 2005)

Whilst similar findings have been reported in the past, there is still merit in providing brief discussion of these familiar themes from the literature here, as these diagnostic narratives align the participants in this study with the wider body of research in this area. Strong parallels between previous work and the testimonies generated here confer dependability and trustworthiness on this endeavour, and provide a solid foundation for subsequent discussion of new emergent themes within these contemporary accounts.

4.3 An illness continuum

Discussion of diagnosis provides a useful basis for gaining insight into how participants positioned and contextualised the disease within their testimonies. Whilst initial reactions to an HCV diagnosis hold up a mirror to society's inter-subjective understanding of HCV and how it has been constructed, the continuing forms in which people go on to experience that disease contributed to a changing perception (Brown, 1995). Reactions to an HCV diagnosis were modified, tempered and revised as individuals experienced the illness, and came to understand it from a new perspective. It is these modified understandings that will now be examined. Embedded within these narratives, an enduring sense emerged of participants constructing HCV as an illness of degrees. The singularity of the diagnostic HCV label disguised a range of illness trajectories and outcomes which gradually revealed themselves during post-diagnosis engagement with a variety of health professionals, support agencies and other individuals with HCV. Participants re-evaluated, reformed and repositioned their understanding of HCV, in light of the experience and health of others, and more significantly in light of the health and condition of their liver. The perception of degrees of HCV was further enforced by the inequality of access to new HCV treatments, as the following analysis will demonstrate.

4.3.1 *Feeling fortunate*

Participants often framed their own experience of living with HCV in terms of how they were faring in relation to others. Their narratives measured and positioned their own

health and the impact of the disease against others who were HCV positive, whether personally known to them or not. The majority of participants recounted their own perceptions of how HCV was having less impact on their life than it was for other individuals. However, tangible examples of this dynamic were few and far between. A broad perception pervaded instead that ‘others have it worse’. Participants described feeling generally fortunate and lucky in comparison to other people:

M: Hmmm, I think, compared to a lot of people with hep C, I have been really, really lucky. You know what I mean?

I: Why?

M: It's not really had that much of an impact on my life day-to-day, you know what I mean? Compared to people with this an' that, an', I can see, no it hasn't. I'm very, very lucky.

(Marilyn, 52, non-cirrhotic)

...I think I've been a little bit lightweight here because, you know, there's a lot of people out there that are, really in much worse chance with hep C than I have, so I'm, you know, considering myself to be quite fortunate...

(John, 54, non-cirrhotic)

A major contributing factor to this perception was often the relative health of their liver compared to others, information which was obtained post-diagnosis from scans and blood tests following engagement with HCV treatment services²⁵. News of their liver's comparative health began to contextualise the diagnosis and fracture their understanding of HCV as a single disease. HCV could be both a malignant killer and a benign inconvenience:

...and I have [the ultrasound scan] done today, and according to the person who did it, I say please I need to know something, I cannot wait another week, she say everything seems to be normal, no damage at all, which I feel like I won the lottery and [pauses] I know it's not, I know many people die of hepatitis C in the past; and it's not that easy to cure, or some people have more complication than other, but to be honest with you, I feel relief knowing that there is no damage in the liver.

(Peter, 51, non-cirrhotic)

²⁵ It is worth noting that for Eilidh, the only participant who had not engaged with HCV treatment services on any level, this discourse was absent.

Examples of feeling fortunate were even present amongst the narratives of those with more advanced liver disease, although these tended to be framed not in relation to other people, but in relation to their own mortality. Despite being cirrhotic, a diagnosis of HCV had given Steve the impetus to make changes to his lifestyle, and his understanding of HCV therefore included elements which were protective and beneficial:

...over three years now I've been sober, d'y'know, err, an' my liver's knackered [laughs] an' it kind a' makes you feel wow – that's, what would I 'ave been like if I was [pauses] - I'd be dead. I would've been dead [laughs], d'you know what I mean? Wow. Y'know, it's like wow, there's no way I'd have survived that, nah, err, so you're thinking well I'm very very lucky...

(Steve, 45, cirrhotic)

By framing their experience in terms of feeling fortunate, the participants were attempting to regain control of their situation, and positively positioning their own health in relation to a worst case scenario. This can be viewed as a discursive strategy, used to construct an identity which emphasises survivorship, supports coping with situational change and locates the individual as strong in relation to weaker others (Harré and Langenhove, 1999b). It also resonates with social comparison theory, which suggests human beings have a drive to compare themselves with similar others, especially in times of uncertainty and stress (Gibbons and Buunk, 1999). Previous work drawing on social comparison theory in other conditions, such as ovarian cancer and motor neurone disease, has demonstrated patients most frequently compare themselves to individuals they perceive to be worse-off, allowing them to view their own situation in a better light, and enhancing their sense of self (e.g. Locock and Brown, 2010; Morrell *et al*, 2012). Such downwards comparisons can increase self-esteem, manage mood, and function as an emotional coping strategy (Carrick Taylor *et al*, 2007). However, there may also be undesirable affects. The following quote demonstrates how Fiona's engagement in social comparison acted as a personal barrier to accessing services and care:

...an' there's far more needy patients in front a' me, y'know, my liver's healthy an', things like that Dave, but that's always my out, y'know, it's like, oh well you've only got one room up in [the respite facility], well give it to that person,

'cause they need it more than me, y'know, I've got a house, I can go home an', it's always that - it's, no Fiona, you need it jus' as much as, y'know, but I'm always like, no, no, gi' it to them, y'know, they need it more than me...

(Fiona, 40, non-cirrhotic)

By socially comparing their situation to others, the participants fractured HCV into degrees. There were those who 'had it worse' or who were 'more in need'. Hepatitis C became a continuum of illness rather than a uniform disease. This understanding was further enforced as participants confronted the inequality of access to new HCV treatments, and came to understand that their position on the illness continuum had direct consequences for their entitlement to new medications.

4.3.2 The disparity of access

As the degree of liver disease has emerged as the central tenet of distributive justice for accessing DAAs in international, national and local guidelines (Pawlotsky *et al*, 2015b; Scottish Government, 2015a), the importance placed on liver health by the participants reflected both a concern for their immediate and future health, but also for their own trajectory of care. Whilst news of a healthier liver conferred a positive prognosis, it could also mean denial to the most effective treatment and could therefore be recognised as a double-edged sword.

For a number of participants, the disparity of access to new HCV drugs created a perception that these medications were for the prioritised few, whose need was greater than theirs. Consequently, participants with mild to moderate liver disease described themselves as almost not requiring treatment at this time, and/or that they were 'too healthy' to gain benefit from the new medications. Treatment therefore remained a task for the future:

I've been had a...the scan done an' stuff, an' they're saying that everything looks alright, I've not got erm, what d'you call it? Thing wi' the liver? Cirrhosis o' the liver or anything, erm, so now they deal wi' that first before, y'know they deal wi' people that are doing alright...

(Kelly, 34, non-cirrhotic)

I: How do you feel knowing that there are treatments out there, but you're not eligible for them?

S: That's fine. Err, no problem wi' that. People who need it should get it, and we can just wait, y'know, until our time comes, err, we have to have it, but no, the people who really need it should have it, that's it.

(Sheila, 59, non-cirrhotic)

I: And, this new treatment...is it available?

K: No [laughs]. I thought it was, but it's not, 'cause the money. My liver's not destroyed enough, err, not sick enough to get treatment now...

(Keith, 54, non-cirrhotic)

For some, the awareness that they were unable to gain access to new HCV therapies was embraced as a positive endorsement of the health of their liver. New treatments were associated with a greater degree of liver damage, and therefore *not* being prioritised to receive interferon-free regimens further affirmed and corroborated the reassuring results previously received from blood tests and scans:

...after doing the test on the [mimes fibroscan®], seeing how the liver is being damaged, I felt a bit like err, relieved in the sense that err, even though I've had hepatitis for a long time, and err, with all the alcohol I've been drinking, the damage was not that bad that I should be put on the priority of the people who are more severe. So, kind of, it was a bit comforting for me.

(Happy, 51, non-cirrhotic)

[the HCV nurse] said the only way that you will qualify for this one, (is) with advanced cirrhosis, and I say oh I rather not qualify. So that, that made me feel better that, if I see it from that point of view, that to qualify for I have to be in a kind of bad stage, so I rather don't go through that because that mean I will have, I have damage.

(Peter, 51, non-cirrhotic)

The denial of new treatments to a few patients resulted in a very different attitude. Within a narrative that discussed a lengthy and hard-fought recovery from drug and alcohol use, combined with a long history of intermittent engagement with HCV

services, Paul recounted his thoughts at being informed he did not meet the eligibility criteria for the treatment he had been working towards for many years:

...an' then (to)day I've sort a' been told that I dunnae fit the criteria, if [pauses] because my liver's quite healthy which is, a bit of a' shock but hey, wait a minute, you want me a' go to start using? Or you want me to, y'know, make mysel' worse so I could, get an easier (treatment)?

(Paul, 37, non-cirrhotic)

Despite sporadic narratives such as this, an acceptance and understanding prevailed that those with a greater degree of liver damage and further along the HCV illness continuum should be treated first, and that this prioritisation was necessitated by financial constraints within the NHS and the costs of the drugs. The acceptance of health inequalities demonstrated within these narratives is symptomatic of the tolerance of rights violations and lack of entitlement, control and power that disenfranchised HCV communities have grown accustomed to over the years (Wolfe *et al*, 2015). It resonates with the work of Rhodes *et al* (2013) who, in their exploration of patient citizenship, described few of their participants positioning HCV therapy as an automatic entitlement. They described how eligibility negotiations served to further distance their participants from treatment, reinforcing perceptions that they were undeserving of care.

The rationalisation and adoption of arguments *for* the prioritisation of HCV treatment was present in the discourse of participants who would not benefit from such treatment rationing. Whilst a weak entitlement to therapeutic citizenship, or the recruitment of a particularly altruistic group of patients may be the reason, the illusory truth effect, which describes the increased tendency to believe information to be correct upon repeated exposure, may also play a role (Fazio, Brashier, Payne and Marsh, 2015). If you tell someone they are not entitled to access new treatments enough, they will eventually believe it.

The common acceptance of this situation amongst the participants contrasts with the global activism demonstrated by patient advocacy groups, which have been highly critical of restricted access policies for new HCV medications and vocal in appealing for

the removal of HCV treatment rationing (e.g. Treatment Action Group, 2016). The disparity between the study participants' acceptance and patient groups' campaigning is curious. Whilst it could signal that a potentially atypical group of participants were recruited, it is perhaps more likely to highlight the atypical nature of individuals who join HCV advocacy movements.

4.3.3 A continuum of merit

The insidious integration of the treatment prioritisation mantra into the participants' discourse continued when discussion turned away from liver health, and distributive justice was discussed in terms of merit, rather than need. These narratives positioned people as less deserving of treatment if they were perceived as likely to waste resources due to ongoing drug and/or alcohol use, conforming to the notion that these individuals were not entitled to parity of healthcare and social participation (Harris, Albers and Swan, 2015):

I: You said if people are still drinking or using drugs then maybe they shouldn't...

K: [pauses] I know, eh, that's a hard one. I, I do believe that if they're still drinking an' that they shouldn'ae be getting the treatment, because it's a waste a' time. It's no' because I dunnae want them a' get better or anything like that, it's jus' 'cause they're wasting resources an' money, y'know what I mean, it's stupid, (...) when you're getting a drug that costs so much, even if it didn'ae cost a lot, it'd still be stupid, y'know you're jus' wasting your time, you're wasting the doctors time, an' really, if you're jus' gonna keep taking, drinking, ken fucking up...

(Keith, 54, non-cirrhotic)

An impression emerged that in order to access new HCV treatments, some work on the part of the recipient should be engaged in with relation to drug and alcohol use. Therapeutic citizenship reproduced an expectation that individuals should engage in self-improvement, becoming more responsible and reliable in order to negotiate their entitlement to treatment (Rhodes *et al*, 2013). Stewart's account referenced this on a number of occasions, positioning himself as more deserving of treatment, not due to the condition of his liver, but because of the way he perceived others were living their lives:

And, to tell you the truth, I fee...sometimes coming here, I feel, pretty broken when I see some people that [mumbles to self as thinks of words], that aren'ae looking after their-selves, I mean I've been sitting here, people have been phoning up like for appointments, an' coming in, an' jus', you jus' know they're no' looking after their-selves an' I'm jus' sitting there, on time, trying a' help myself, fed up, an' it jus' sometimes, blows you away that, why are they getting treated better than me eh?

(Stewart, 52, cirrhotic)

...but then there's, the other side is [pauses], if you're a, if you're a [whispers to self: oh God] if you're a drug user, then, if you know the risks, you must know the risks [pauses], something like that that's jus' bad thoughts like; [takes deep breath] they shouldn'ae be as high as the list. That's jus' my thoughts on it like.

(Stewart, 52, cirrhotic)

Concurrent narratives of distributive justice by need and merit could sit side-by-side within a single participant's account, with little sense of conflict. This is perhaps unsurprising, as beliefs about justice are often pluralistic, in the sense that they cannot be accounted for by reference to a single basic principle of distribution (Miller, 1992). Rather, individuals typically invoke several criteria and reach an overall judgement by considering these criteria against each other. A complex social understanding of HCV treatment allocation is therefore evident within these narratives. Individuals balance need, merit, and other factors against a perception of their own position on the HCV illness continuum, whilst adopting an almost unquestioning tolerance of inequality.

4.3.4 Theme summation

The theme 'positioning hepatitis C' resulted from a compelling thread which wound through the collected narratives. Beginning with the accounts of diagnosis, HCV was constructed by participants as a contextual illness, positioned in relation to wider socio-cultural, medical, and politico-economic contexts. For those diagnosed within a period of drug use, the reaction to being HCV positive was moderated and tempered by a pre-existing social diagnosis of 'pre-HCV'. Other comorbidities were also employed to provide context to the disease, with HIV and cancer consistently positioned as more significant diagnoses. Of note, the timing of diagnosis in relation to advances in HCV treatment did not impact on participants' understandings of the disease, or responses to it.

Following diagnosis, participants described a repositioning of other aspects of their lives in relation to HCV. Transformation narratives wove through the discourse as alcohol and drug use were reconsidered. Slowly, a changing perception of HCV became evident for those who had engaged with HCV services. Participants described multiple experiences of HCV, which fractured the understanding of a singular and uniform disease into a continuum of illness. Hepatitis C was positioned within the narratives in relation to others with the same disease, the comparative health of their liver, and the discourse of distributive justice which accompanies the arrival of interferon-free therapy.

Chapter 5

Beyond a physical burden

5.1 Introduction

This chapter aims to explore how participants predominantly situated the impact of their HCV infection within the mental and emotional, rather than physical, dimensions of illness. The emotional burden of HCV formed a central and crucial theme within their narratives, which differed from the transient and irregular influence the infection demonstrated on their physical health. To illustrate this disparity, this chapter primarily focuses on two enduring motifs of HCV: fatigue and stigma. The discourse surrounding fatigue is considered first, and the weak and insubstantial pattern it produced within the data revealed. In contrast, the clear and compelling construction of HCV as a psychological burden is then explored, with an emphasis on the continued significance of stigma to the inter-subjective lived experience. This discussion of stigma explains the concept of 'felt' stigma, and provides insight into how felt stigma was produced and embodied within the narratives. It then identifies strategies which the participants used to manage their discreditable identity. The experience of felt stigma is then contrasted with how incidents of 'enacted' stigma proved relatively rare, and how disclosure of their HCV status often met with an unexpectedly positive response. The importance the participants placed on emotional support is then addressed.

This chapter reveals how the participants firmly located the psychological burden of a somatic disease as their predominant concern. In doing so, it emphasises that whilst the much vaunted developments in HCV drug therapy are clearly important in eradicating the virus and improving treatment outcomes, they do little to address the components of the daily lived experience which matter most to those infected. The findings from this study suggest that stigma, and the emotional (felt) burden of illness, have not reduced in the current era of more effective treatment. Concurrent strategies for challenging the ongoing and deep-seated stigma associated with HCV must therefore form a vital element of any patient-centred global response to the disease.

5.2 A physical affliction?

5.2.1 Fatigue

The impact of HCV on the physical health of those infected has received significant attention in previous studies. Fatigue has been cited as the most important contributing factor in reduced HRQoL (Kallman *et al*, 2007), and has formed an enduring theme in qualitative work focused on the experience of living with HCV (Conrad *et al*, 2006; Fry and Bates, 2012; Glacken *et al*, 2001; Glacken *et al*, 2003; Groessl *et al*, 2008; Sutton and Treloar, 2007). The emphasis that fatigue has received within the scientific literature made it an expected theme within this study, and whilst the physical impact of HCV *did* feature in a number of the participants' narratives, it did *not* form a compelling analytical refrain.

Indeed, the physical aspect of HCV infection was absent from almost half of the participants' testimonies, and where it did occur, the primacy which fatigue has commonly been assigned was not in evidence. The discourse of physical disruption was rarely emphasised as particularly significant, with reduced energy and general fatigue mentioned anecdotally, and framed by most as a manageable and slight inconvenience, rather than as a life-changing disorder:

No, I jus'...I jus' feel [pauses] a little bit drained but not sick, sick. My body's jus' went through like a, a big deal, y'know, a big thing, that's it, but I don't feel like - oh my God, y'know, I'm dying, I'm dying, y'know...

(Anita, 46, diagnosed 2014)

References to fatigue were found in the narratives of those who described their liver as cirrhotic, but also in the testimonies of those with a lesser degree of liver disease. There were no clear associations with any of the participant demographics. Fatigue appeared sporadically and infrequently in some narratives, and remained entirely absent from others, producing a fragile and insubstantial candidate theme during the analytical process (Braun and Clarke, 2006). The vast majority of participants constructed accounts which primarily made reference to *not* feeling especially exhausted or noticing any particular physical symptoms, with many speaking about the ordinariness and normality of their daily life:

I dunnae really, aye, I dunnae focus much on it, an' then when I do think about it, I think well, it's no' like it changes my lifestyle or, y'know there's things that I cannae do, I can still live a normal life an', aye...

(Kelly, 34, diagnosed 2008)

I: Does [HCV] stop you doing anything?

G: I've not found that, as yet. Jus', my normal problems that I have anyway jus'...just, balance it so I wouldn't (...) I wouldn'ae say that it's [pauses] nah, I wouldn't say that it has at all, hasn't stopped me from getting anywhere or doing anything.

(Gary, 38, diagnosed 2013)

5.2.2 A disproportionate focus

The absence, or relative insignificance, with which fatigue was framed within the majority of narratives demands further attention. Fatigue has been described as the most frequent extrahepatic manifestation observed in individuals with HCV in both quantitative and qualitative investigation (e.g. Lang *et al*, 2006; Poynard *et al*, 2002). Therefore, its marginal influence within this study is curious. It is, however, not unique. In a recent phenomenological study, Hill *et al* (2015) considered fatigue only briefly in one of their six themes describing the experience of living with HCV during the interferon-era, with their themes predominantly focused on the psychological impact of the infection. Of note, they conducted unstructured interviews with their participants, opening with just one question: “can you tell me how it has been for you, living with hepatitis C?” Similarly, the interview schedule within this study did not address fatigue explicitly (appendix C), and this manifestation of HCV was only discussed if the participants specifically made reference to it within their discourse.

It could be argued, therefore, that where fatigue is looked for, it will be found. This focus on the symptom does not necessarily equate with its significance to those infected with the virus. For example, quantitative investigation of fatigue uses patient-reported outcome measures such as the Fatigue Severity Scale or the Brief Fatigue Inventory, in order to study fatigue based on a priori assumptions about the population they are investigating (e.g. Fabregas *et al*, 2013; Kallman *et al*, 2007). Qualitative research is not immune from this approach either. A recent study

investigating HCV patients' experience of fatigue used criterion sampling to interview only those individuals who had previously reported clinically significant fatigue on the Fatigue Severity Scale as part of another study (Zalai *et al*, 2016). It is possible that this investigator-led focus on fatigue has created a disproportionate wealth of literature on the topic, which in turn reinforces its reputation as one of the most significant patient-reported outcomes of HCV infection.

A further consideration arises. Has the emphasis which has been placed on fatigue, both within the scientific literature and subsequently within clinical practice, resulted in a self-fulfilling prophecy? The awareness that HCV and fatigue have been constructed as inseparable bedfellows provides a convenient hook on which to hang a physical symptom which may also be explained by consideration of numerous other factors. The following quote illustrates this well. After identifying a number of influences which could have accounted for her constant exhaustion, Fiona instinctively aligned her symptoms to an (as then) undiagnosed HCV infection:

I was jus' constantly tired, erm, my immune system was run down a lot, but I jus' thought it was bad living, taking drugs, not eating well, going out five in the morning, doing my job, things like that, I mean, basically jus' not thinking it could a' been anything like [HCV]...

(Fiona, 40, diagnosed 2012)

Whilst fatigue formed a significant aspect to the lived experience of HCV for a small minority of individuals within this study, it was not the all-encompassing and unifying experience that previous studies have proposed. In focusing on the life-world of the participants, and describing and interpreting those aspects of the lived experience constructed as the most significant by the participants themselves, this study questions the centrality commonly attributed to fatigue in the lived experience of HCV.

5.3 An emotional illness

5.3.1 Always on my mind

Whilst the physical burden of HCV formed a weak and insubstantial pattern within the data, the impact on the participants' psychological health was richly constructed and comprised multiple strands. Hepatitis C was framed as an illness which caused a

persistent disquiet and underlying worry. It was frequently described as occupying a permanent space at the back of participants' minds, producing a constant unease which they tried not to dwell upon or brood over:

I don't, I don't, I try not to obsess about it, you know, it's kind of running away in the back of your mind the whole time but I try not to you know, let it kind of affect me too much...

(John, 54, diagnosed 2012)

I: How do you cope with having hep C Jacqueline?

J: [pause] to tell you the truth, to be honest, I can't, I can't cope with it. I'm having a job coping with it. I don't like to, I know it's got to get mentioned now'n again, but I'd rather put it [indicates the back of her head] back...

(Jacqueline, 70, diagnosed 1991)

The lack of physical impact from HCV contributed towards this enduring worry at the back of their minds. Whilst some participants used the lack of symptoms to try and block HCV from their thoughts, others found being unable to monitor the effect HCV may be having on their body unsettling. The idea that HCV might be doing something *"that I can't see, I can't feel, I can't detect"*²⁶ produced its own set of anxieties and concerns, which fed the underlying psychological burden.

In addition to this tenacious and unrelenting torment at the back of their minds, the participants related specific factors which served to bring this underlying disquiet to the fore. The fear of transmitting the virus to others was framed as a significant source of anxiety. However, the greatest psychological burden was evident in the participants' narratives of stigma. Each of these factors will now be examined.

5.3.2 Onward transmission

The majority of participants expressed significant concerns over the risks of passing their HCV infection onto others. Specific fears over transmitting HCV to children and partners were commonplace, and the potential risk to the health of close family and

²⁶ Sheila, 59, diagnosed 1991

friends formed a central concern. The discourse surrounding onward transmission was compelling and consistent, with the narratives accentuating how this was not a periodic and irregular anxiety, but one which influenced their lives on a daily basis:

I struggle wi' it, I struggle wi' jus' being around people an', an' jus' knowing that I could put them at risk, it's jus' a worry, I worry, a day a' day worry...

(Eilidh, 39, diagnosed 2013)

The protection of others from contracting their HCV infection was constructed as a fundamental component of the lived experience. Fictional 'what-ifs' were routinely presented within the discourse to underscore the imagined horror that would be felt should the worst come to pass, with the act of accidentally cutting themselves recurrently presented as a nightmare scenario. Whilst the majority of participants described exercising proportional caution and risk avoidance in relation to identified risks, Anita accentuated her fears of onward transmission by suggesting she had effectively placed her life on hold as a result:

I've always had that thing where I'm so scared that, erm, if I cut myself, y'know, being very wary, y'know, around people (...) and that's why I've, basically I've put my life on hold because I'm like, I am not going to put anyone at risk, so like, like going, an' doing a job or whatever, an' put someone at risk, that's something that I'm, I'm so scared about...

(Anita, 46, diagnosed 2014)

Anxiety over onward transmission also exerted a significant toll on a number of the participants' sexual relationships. Despite a general awareness of the relatively low risk of sexual transmission, an understanding prevailed that this was not a risk to be taken lightly, or indeed a risk worth taking at all. This discourse was more pronounced amongst the single participants, who spoke about deferring the search for a long-term partner and often avoiding casual sex entirely:

I jus' thought, well that's my life ruined, y'know, err, an' since then, I've never, I've never even been wi' another woman, again, that's it. Since I got divorced, that was it, I jus' thought, nah, I can't. Y'know, an' that's been over, I don't know, seven year? I jus' thought well you cannae have sex again, 'cause you'll end up likes, giving it to somebody else.

(Steve, 45, diagnosed 2005)

The psychological burden presented by the fear of onward transmission within this study is consistent with that described in previous investigations into the lived experience of individuals with HCV (Conrad *et al*, 2006; Fraser and Treloar, 2006; Grundy and Beeching, 2004; Temple-Smith *et al*, 2004). Whilst the emotional toll from this hypothesised scenario was clearly evident, it was the discourse surrounding stigma which presented participants with the source of their most significant distress.

5.3.3 Stigma

5.3.3.1 Theoretical basis

That HCV is a highly stigmatised disease has been a stubborn and consistent refrain throughout the scientific literature for many years (see chapter 2). The theoretical basis for much of this discussion has been founded on Erving Goffman's (1963) enduring theory of social stigma. Goffman defined stigma as a discrediting 'mark' or attribute which is socially devalued, and sets an individual aside as a deviant, rather than as a 'normal' member of society. As such, Goffman clearly defined stigmatisation as an interactive social process, where the reaction of others 'spoils' an individual's identity. However, Goffman noted that not all stigma are equally discrediting, since some 'marks' or attributes are less visible than others. He proposed that stigma incorporates two key aspects: the visible (discredited) identity and the invisible (or discreditable) identity. These terms refer to the visual conspicuousness of the stigmatised attribute (Chaudoir, Earnshaw and Andel, 2013), with the discreditable identity resonating with the transient and non-specific physical manifestations often found in individuals with HCV.

The concept of stigma can be further delineated between 'enacted' and 'felt' stigma. Enacted stigma encompasses the overt discrimination against those who possess the socially devalued 'mark' on the sole grounds of their social unacceptability, and 'felt stigma' denotes both a sense of shame and/or an attendant fear of encountering enacted stigma (Scambler, 2009). This dichotomy was developed in work conducted with people diagnosed with epilepsy during the early 1980s, which found many individuals expressed the view that their condition was highly stigmatised, despite being unable to provide actual instances of this stigma operating against them (Scambler and Hopkins, 1986). The following section of analysis takes these concepts

of stigma as a theoretical basis. It begins by examining how felt stigma was constructed within the narratives, exploring the close association between HCV, drug use and HIV/AIDS. Strategies for managing the HCV discreditable identity are then considered. Finally, the felt stigma experienced is contrasted with accounts of enacted stigma, and the discrepancy between the perceptions and experiences of HCV stigma found amongst the participants' narratives highlighted and discussed.

5.3.3.2 Felt stigma

The concept of felt stigma incorporates two predominant components: fear and shame (Scambler, 2004). For a discreditable disease such as HCV, fear arises from the possibility of being treated differently, labelled or 'found out', and is referred to as anticipated stigma within much of the scientific literature (e.g. Quinn *et al*, 2014). The other component, shame, is often considered self-stigma or internalised stigma. In this case, the self-concept of individuals with the stigmatising 'mark' is congruent with the (expected) stigmatising response of others, accepting their discredited status as valid (Scambler, 2009). In short, internalised stigma reflects stigma directed at the self, from the self (Chaudoir *et al*, 2013). This internalised shame was evident in the way participants spoke of how their HCV infection made them feel. They recurrently employed phrases such as 'dirty', 'branded' and 'like a leper', with one participant describing how she felt she had "*beasties crawling about in my bloodstream*"²⁷. For Stewart, the intensity of this internalised stigma had led to external physical manifestations of how unclean and polluted he felt:

Once, a couple a' months ago, thinking about it, I start scratching, I start – oh, I'm no' bothered brushing my teeth today, I dunnae need to do it, what's the point when I've got this?

(Stewart, 52, diagnosed 2015)

Similar insights from studies focused on individuals with HCV have been reported for many years, with participants habitually describing themselves as contaminated, dirty and leprous (Glacken *et al*, 2001; Grundy and Beeching, 2004; Hill *et al*, 2015; Miller *et al*, 2001; Sutton and Treloar, 2007; Zickmund *et al*, 2003). Such findings illustrate how

²⁷ Fiona, 40, diagnosed 2012

HCV challenges the normative and powerful ideal of the pure, closed and clean body²⁸ (Fraser and Treloar, 2006), and demonstrate how individuals with HCV accept and internalise their spoiled identities. That this discourse persists unchanged and unchallenged throughout the body of work conducted in this area, and remains an enduring motif of the lived experience of HCV within the current study, stresses the ongoing strength of HCV stigma within society. Why this may be so can be illuminated by exploring the frequent associations drawn by the participants between HCV and drug use, and HCV and HIV/AIDS.

5.3.3.3 Hepatitis C and injecting drug use

The participants' narratives drew recurrent associations between the internalised stigma they felt as a result of their HCV infection, and predominant societal attitudes towards drug use and PWID. The two were often indissoluble within their discourse, framing HCV as a disease which afflicted PWID, and often placing all those with the infection within this socially vilified group:

I think most people jus' treat hep C as a, as just a dirty, dirty, disgusting virus...an' I think most people (...) jus' think you're a bloody drug user. It's, that's the way most people think.

(Stewart, 52, diagnosed 2015)

For those participants who had moved on from a drug-using past, HCV provided an unwelcome reminder of those bygone days. It served to resurrect the stigma they had encountered during their period of addiction, and brought back memories of an old life which they had tried to leave behind. The sense of shame and embarrassment felt at a drug-using past was revived and galvanised by the arrival of HCV in their lives.

Hepatitis C was a badge of dishonour, a relic of a life once lived:

It's just err, it's the same as when I, I mean I dunnae wear T-shirts because I've got track marks, old, old scar marks fae injecting an' stuff [indicates arms] it, jus' that old life y'know, an I've moved away fa' that, an' I'm real, I mean I'm like seven year off, off heroin an' that, I've been clean for a lot a' years (...) But like I say, I do feel a sense, I am ashamed a' myself through the hep...

(Paul, 37, diagnosed 2000)

²⁸ An ideal which ignores the frequent ingress of micro-organisms to the human body, and the permanent presence within the body of beneficial flora (Fraser and Treloar, 2006).

...it kind of reminds me of some of the horrific things that happened whilst I was using [pauses], erm, not, yeah – not proud, you know, distinctly not proud looking back...

(John, 54, diagnosed 2012)

In addition to this internalised shame, the participants also produced narratives which were replete with anxieties and fears regarding how disclosure of their HCV positive status would indelibly connect them with drug use in the eyes of friends, family and wider society. This anticipated stigma was evident within the discourse of those who did not identify as people who use drugs (PWUD) (see the quote from Stewart above for example), but also for those who readily divulged an extensive drug-using history. This perhaps surprising insight echoes previous work which challenged the common-sense notion that PWUD have little concern for what others may think of their behaviour (Simmonds and Coomber, 2009):

I guess again, that, that sort a', that stigma around it, I don't want people thinking that it's something that it isn't, like if you tell people "oh, I've contracted hep C" y'know, there's potential that they're gonna think that you're y'know, knee-deep in drug use, y'know you're like a complete junkie, everything like that.

(Dan, 27, diagnosed 2013)

Dan framed himself as a recent, but former heroin user. He repeatedly stressed that he had never injected heroin, and vigorously positioned himself apart from those who had. Other participants gave similar testimonies, differentiating between activities which constituted acceptable and unacceptable drug use. Steve described his drug use as *"a lot of cocaine, a lot a' speed, but that's like a party drug"* and distanced himself from heroin use, which he categorised as *"a filthy drug"*. For Fiona, despite her mother being aware that she smoked heroin, the act of injecting the drug was framed as a source of particular shame:

Y'know, it's like oh you've gotta be a junkie a' catch hep C. So it was bad enough knowing my mum knew that I was a heroin smoker, I, I mean I was scared a' needles, I was never ever a heroin injector, I was always just a smoker, so straight away it was like, she's gonna think I've been injecting...

(Fiona, 40, diagnosed 2012)

These narratives produced an understanding that amongst those who identified as PWUD, the stigma surrounding *injecting* drug use was of a significantly greater magnitude, and it was this weightier stigma that conflated with HCV. Hepatitis C did not just designate you as a generic drug user, it branded you an *injecting* drug user. That stigmatisation impacts both *on* drug-using populations and also operates *within* drug-using groups has been noted in numerous previous studies. Furst, Johnson, Dunlap and Curtis (1999) detail a long history of PWUD denigrating other PWUD as a discursive strategy to raise their social status. For example, they describe how cocaine users would call themselves ‘base smokers’ to avoid the stigmatised category of ‘crack head’ in the 1990s. More recently, Simmonds and Coomber (2009) described a hierarchy of stigma within PWID based on perceptions of responsible versus irresponsible behaviour, and upon the type of drug injected. The catch-all terms of ‘PWUD’, ‘PWID’ and ‘substance users’ belie the complex social hierarchies that can exist within drug-using communities, and the degrees of stigma which specific types of drug taking can attract.

5.3.3.4 Hepatitis C and HIV/AIDS

In addition to drug use, over half the participants entwined their discourse concerning the stigma of HCV with understandings of HIV/AIDS. For many, the two had been synonymous upon diagnosis, and only on subsequent engagement with HCV services had the difference between these viral infections become clear. Whilst some participants had known individuals with HIV/AIDS, and others mentioned infamous HIV media campaigns from the 1980s, it was ultimately unclear how this understanding had originated:

I think I took it on that it was more to do with HIV than hep C, I didn't know it was like, two separate things, I actually thought that if I had hep C then I had HIV as well, for so long I thought that way...

(Danielle, 43, diagnosed 2009)

...but when I found out, I was horrified. 'Cause I thought it was the same as AIDS, in my head, it's like, it was like, when somebody says hep, hepatitis C an' you're thinking "it's like HIV" y'know, it was jus' in my head, so I was horrified, an' it destroyed me. Y'know?

(Steve, 45, diagnosed 2005)

Previous studies have also reported this intimate association between HIV/AIDS and HCV, emphasising the additional negative stereotyping which can result (Lekas, Siegel and Leider, 2011). A societal understanding which positions HCV and HIV together also conflates the stigma which accompanies each of these infections. Hepatitis C can therefore invoke prejudice more commonly directed at people living with HIV, such as accusations of sexual promiscuity or association with socially devalued groups such as gay men (in addition to PWID as previously discussed) (Zickmund *et al*, 2003):

...oh if you've got hep C you must be taking drugs or injecting...or gay, y'know, things like that...

(Fiona, 40, diagnosed 2012)

Significantly, stigma associated with HIV has been described as more pervasive and detrimental to wellbeing compared to HCV-related stigma (Lekas *et al*, 2011), a contention supported by the narratives of those HIV/HCV co-infected participants in this study. For the mono-infected group, a vehement desire to dissociate themselves from a potentially greater source of stigma was evident in a number of the participants' accounts:

I've had people coming up to me an' asking me "Phil, are you HIV?" an' I've said "Erm, no I dunno who told you that but I'm, I'm H.C.V., I've got hepatitis C, OK, not HIV, I'm not HIV, don't get that wrong, don't make that mistake, alright?"

(Phil, 60, diagnosed 1997)

5.3.3.5 Managing a discreditable identity

Most participants sought to manage their discreditable identity by strategically and cautiously selecting who they would confide in. The majority of participants acknowledged these acts of concealment were driven by fear of the reaction they may receive (anticipated stigma), and were found in the narratives of those who had no history of drug use, as well as those who identified as PWID:

An' people didn'ae, people used to hide a lot a' things, because, I mean it was still spoken about but I think there was a lot a' people that wouldn'ae have

turned around an' says that I've got hep C because then people wouldn't have wanted to share anything, so I think that's what it was...

(Danielle, 43, diagnosed 2009)

Selective disclosure served to maintain the participants' social status amongst their peers, and gave them a sense of control, allowing a vestige of 'normal' life to continue. However, a discourse was also evident in a number of narratives which presented these selective disclosures nobly, in terms of concern for others:

...y'know I could have told them and they would have understood, erm, but I chose not to, I chose not to tell a few people, jus' because I didn't want to complicate their lives really, to be honest, my dad for one, my mother-in-law...

(John, 54, diagnosed 2012)

Although allowing a sense of control, this selective strategy could also carry an emotional cost of its own. Guilt and remorse at the deception of close friends and family were felt regularly, and voiced frequently. In addition, Happy recounted how concealing her HCV diagnosis from potential partners had resulted in a broken relationship and a stalled social life:

...when I'm meeting people out there, you never know, that's why I'm just like now, I broke up with that guy in [names city], and my social life is on hold, 'cause it's just, it's like I've got this secret in me, yeah? Like when I meet somebody, how, how, how do I say, hmm, by the way...! So for me, I've just blanked [relationships] out...

(Happy, 51, diagnosed 2005)

In addition to simply disclosing or not disclosing their HCV status, a small number of participants engaged in practices which conveyed the fact they were unwell, but which avoided specific mention of HCV. For example, Fiona spoke to friends about her hospital appointments, but ascribed them to other conditions. Peter counselled his family that his "*blood was being poisoned*" without further elaboration, whilst Gary avoided any mention of blood or viruses at all:

I wasn't lying I just never said that I had hepatitis C, I jus' said listen, my liver's knackered, there is a chance a' having cirrhosis, if I don't get it treated. And I

kind of jus' left it at that, nobody seemed to come back with oh, you've got this, or you've got that, they were quite happy with that...

(Gary, 38, diagnosed 2013)

This strategy of disguised disclosure sought to maintain control over their discreditable identity and provide protection from stigma, whilst also allowing access to help, support and sympathy from friends and family. As the narratives progressed, however, this approach was rarely successful. Fiona became embroiled in ever more elaborate lies, and the internet soon provided Peter's family with the specifics he had failed to deliver.

For a further small number of participants, managing a discreditable identity was tackled head on by disclosing their HCV status widely. It was better to be open and honest with everyone than contend with the complexities of selective or disguised disclosure. Participants justified this uncompromising approach by emphasising the personal gain to be achieved ("*opening up does help*"²⁹; "*I tell people right up front 'cause I dinnae wanna waste time wi' somebody who's gonna be my fair-weather pal*"³⁰), and by citing altruistic intentions. Anita positioned herself as a cautionary tale:

I'm straight up with people, y'know, because if I can sort a' make someone think y'know, hey, I'm no' away a' do that, then, yeah, I'll, I'll, I tell people.

(Anita, 46, diagnosed 2014)

Whilst the intentional transformation of a discreditable identity into a discredited one may seem a surprising strategy, previous research suggests that internalised and anticipated stigma may be similar for both discreditable and discredited identities (Chaudoir *et al*, 2013). Indeed, some studies suggest that internalised stigma may be greater for those with concealable stigma than those with a discredited one (Cook, Arrow and Malle, 2011). By adopting this approach, participants weighed the risks of encountering greater social devaluation and enacted stigma against the potential benefits of reduced psychological distress and internalised shame.

²⁹ Stewart, 52, diagnosed 2015

³⁰ Keith, 54, diagnosed 2004

A further strategy for managing a discreditable identity was evident within the narratives. Participants disparaged and criticised those who were anticipated to hold stigmatising views, and in doing so sought to enforce a discreditable identity *on them*. These individuals were frequently referred to as ‘small-minded’, ‘uneducated’ and ‘ignorant’, terms which carry a socially devalued status, and positioned the people using them as more understanding, progressive and enlightened. The participants launched a pre-emptive discursive attack:

...but that's small-minded people, that's the way I see it, I, if you're that small-minded to think like that then, you, you think like that 'cause there's people out there that dunnae think like that, d'you know what I mean?

(Eilidh, 39, diagnosed 2013)

...you know what you've got, an' you accept, you accept it. Anybody else doesn'ae wanna accept it, then, they're no' worth talking to, simple as that. That's how I look at things.

(Dean, 54, diagnosed 1997)

5.3.3.6 Enacted stigma

Enacted stigma refers to the degree to which individuals have experienced discrimination or social rejection as a result of their discrediting ‘mark’ (Scambler, 2009). Whilst the participants constructed narratives rich in anxiety concerning anticipated stigma, and replete with accounts of internalised shame, discussion of first-hand experiences of stigma were often hard to pin down. Participants spoke of “*seeing stigma about*”³¹, but when pressed for specific details of their personal experiences often reverted to speaking in generalisations and relaying generic second-hand accounts. For example, Gary’s description of enacted stigma positioned him as an observer to a stigmatising practice, rather than as a direct recipient of discrimination:

...people just have it on automatic assumption, to what it is, and how it's gon' affect you an', I've seen people say "ooo, can't touch you, 'cause you're infected" an' it's jus' like silliness.

(Gary, 38, diagnosed 2013)

³¹ Fiona, 40, diagnosed 2012

That is not to say primary accounts of enacted stigma were not present. A small number of participants related specific occasions where they had encountered discrimination from family, friends or co-workers. The majority of these anecdotes were framed as rare, one-off episodes, transiently troublesome but a relatively minor annoyance. However, for Jacqueline, a more profound and long-term negative psychological outcome was apparent:

...these friends, they actually make me feel as if [pauses] I'm like, not say like an alien but like, they're further away from me than they used to be that close, y'know? They always used to say oh, give you a cuddle cheerio an' now they don't do that y'know, an' I think that, I don't think they realise how much that hurts, y'know to think that that's what they could catch.

(Jacqueline, 70, diagnosed 1991)

For those participants who disclosed a history of incarceration, the prison setting featured as a significant source of enacted stigma in their narratives. The participants' testimonies recounted anecdotes of fellow prisoners refusing to share a cell, or stand next to them in a queue for the dining hall, and constructed prison as *"the worse place to ever, ever have it"*³². Enacted stigma within the prison setting was constructed as commonplace, unexceptional and routine, invading every aspect of the participant's life and experienced on a daily basis:

...they wouldn't go in the shower cubicle you had jus' come out a'. An' you could actually see them looking around an' going into another one, d'ya know what I mean? Or physically waiting, if I come out the shower, an' there was like guys, maybe going for visits an' stuff, an' the other showers were full, an' seen me coming out they'd go a' go in an' then, they'd stop an' they'd stand, an' then another guy would come out an' they'd go into that one. An' it's because people knew that I had hep C...

(Keith, 54, diagnosed 2004)

This study did not seek ethical approval to recruit individuals who were incarcerated. However, the findings suggest a notably different experience of enacted stigma within the prison setting than found more generally within the community. Further research

³² Steve, 45, diagnosed 2005

specifically focused on the experience of stigma by incarcerated HCV positive individuals would help elucidate this phenomenon.

Whilst considering enacted stigma within institutional settings, the relative absence of stigmatising behaviour from healthcare professionals within the collective discourse was notable. Previous studies have repeatedly described the healthcare setting as a frequent source of enacted stigma (Butt *et al*, 2008; Fry and Bates, 2012; Grundy and Beeching, 2004; Hill *et al*, 2015; Janke *et al*, 2008; Miller *et al*, 2001; Sgorbini *et al*, 2009; Temple-Smith *et al*, 2004; Tompkins *et al*, 2005; Zickmund *et al*, 2003), yet only one participant, Kelly, recounted anything other than praise for the care they had received:

...the nurses put me in a wee side room, an' then they were coming in, they were putting on masks an' err...pinny-things o'er their, their...uniform an', err, washing they hands an' putting like two sets a' gloves on an', an' it was horrible, an' it would've been on my form, my, records an' stuff about me having it (...), even the auxiliary nurses, erm, weren'ae come to my door or anything, know they used to come round wi' like, tea an' toast an' stuff, it was like they were missing me out deliberately an' stuff eh?

(Kelly, 34, diagnosed 2008)

That accounts of healthcare related stigma such as Kelly's were a scarcity within the discourse should not be taken as evidence that stigmatising attitudes towards HCV patients amongst healthcare staff are changing. All participants in this study were recruited through their healthcare team, and the majority were interviewed within an outpatient clinic. Despite assurances of confidentiality and anonymity, participants may have consciously edited their narratives to avoid any possibility that reports of stigmatisation by healthcare staff would be attributable to them. In addition, the outpatient clinic which provided the main recruitment location may have presented an atypical experience of healthcare related stigma, given that it was an infectious diseases unit which specialised in treating marginalised groups:

...the horror stories I've heard of other places, I've not experienced it because I've not had another hospital apart from here, so I jus' think everything's great, y'know, but the stories that I've heard are pretty bad, an' that kind a'

put me really off, I was like wow, I'm glad I didn't have to go to them hospitals, y'know, so I was very lucky that I ended up [here]...

(Steve, 45, diagnosed 2005)

Of note, Kelly did not attend the outpatient unit which served as the main recruitment site, and was interviewed within her own home. Her account of healthcare related stigma also took place on a general hospital ward, where she had been admitted for reasons unrelated to her HCV infection. All these factors may have contributed to the ease with which Kelly related this anecdote.

5.3.3.7 An unexpected response

Whilst sporadic reports of enacted stigma featured in a number of the participants' narratives, the overwhelming impression of other people's reactions to their diagnosis was a positive one. Over half the participants recounted how family, friends and acquaintances had taken the news that they were HCV positive in their stride, offering non-judgemental support and challenging the expectation of a negative response:

...so my mum was a lot more understanding than I thought she would a' been, I thought she would a' been really angry – right, that's it, y'know, I've seen this, sort a', dirty, she's been doing more than she's letting on for her a' have this kind a' disease, 'cause this is, sort a', somebody, that takes drugs, so she's gonna have caught that through taking drugs - so I thought that she would a' had that view, an' she really didn't, y'know, an' neither did my brother...

(Fiona, 40, diagnosed 2012)

This positive reaction was evident not just from close friends and family members, but in wider social circles. Encounters which had been supportive and encouraging were related by those who had also recounted experiencing episodes of stigmatisation, in order to set their negative anecdotes into context. After discussion of the strains of prison life with HCV, Steve was quick to acknowledge that everyone else he had confided in “*were fine about it, y'know. They were much more understanding than you think, y'know, it was like, yeah, that was cool*”. Where disclosure to individuals who may have been at risk of transmission occurred, participants described receiving a grateful response, with people thankful for letting them know:

I: And what sort of reactions have you had?

E: Appreciation.

I: That you've told them?

E: That I've told them, aye.

I: Who's that from?

E: Like people that I've used wi', like obviously my kids dunnae understand, err, so, so they're busy – thanks for telling me mum – like other people that I've used, used wi' an' ken like they're quite appreciative that, that I've told them that.

(Eilidh, 39, diagnosed 2013)

Given the earlier discussion of stigma operating *within* drug-using groups, this insight from Eilidh is perhaps surprising. Where a negative and stigmatising response could have been expected, she recounted gratitude and appreciation from drug-using acquaintances for being informed. Eilidh's discourse alludes to the presence of a moral code among her peers, where stigmatising responses may have been constrained by her consideration of their welfare. Eilidh's disclosure allowed others within her social circle to exercise caution, and resonates with other literature which has examined the etiquette surrounding the order of injecting in a socially interactive context (Crisp, Barber and Gilbertson, 1998; McElrath and Harris, 2013).

5.3.3.8 Covert enacted stigma

This analysis of the discourse surrounding stigma suggests a significant discrepancy between the stigma *felt* by participants, and actual reports of stigma operating against them. Whilst this could imply that the participants' experiences of felt stigma were out of proportion to the level of stigma found within society, the narratives of a few participants also hinted at another explanation.

Enacted stigma is commonly framed within the scientific literature as the experience of *overt* discriminatory practices, which are episodic and discrete in nature (e.g. Lekas *et al*, 2011; Scambler, 2009). This framing produces an impression that enacted stigma occurs solely in memorable instalments, where specific instances of observed

discrimination and prejudice stand out in the participants' minds. The previous quote from Kelly describing her experience on a hospital ward illustrates this well. It is this perception of enacted stigma which initially guided the analysis of this section of data, scouring the narratives for specific examples or striking anecdotes of observed discriminatory behaviour. Enacted stigma, however, was not always so explicit. Within his narrative, Keith touched on experiences of stigma which were often more covert and unremarkable:

An' people'll not sit beside you or, y'know what I mean (...) an' you, you can, you can feel, you can actually, it's physical, you can actually feel people moving away from you, y'know what I mean?

(Keith, 54, diagnosed 2004)

Such accounts allude to the passive nature of much stigmatising practice within society, which may often go unnoticed or be disregarded by those it targets. Enacted stigma is not always overt and notable, but pervades daily life in ways which have become so routine and commonplace that they are no longer noteworthy or noticeable, and therefore remain largely unreported. Keith was attuned to such acts of covert enacted stigma, but because similar accounts were absent from the majority of other participants' narratives, is it safe to assume such incidents never occurred? Accounts of enacted stigma were rare within the discourse, because participants looked for occurrences of discrimination which were *overt*, above and beyond the accepted, and often unseen or unnoticed incidents that formed a part of their daily lived experience.

Stigma could also be enacted against individuals remotely in ways which were not directly observed and would therefore also remain unreported. Eilidh related how a chance encounter with an acquaintance revealed a concealed act of discrimination which may otherwise have gone undetected:

...there is a woman doon at the shops, erm, she used a' go a' the [community centre], now she's got a cup in the [community centre], an' she stood at the bus stop – now I never told her I'd hepatitis C, 'cause I, I dunnae use or that wi' her, I dunnae take drugs an' that wi', so I never had the need to feel that I had

to say to her well I've got hep C – she's standing at the bus stop "aye, fuckin' I'm gonna get my cup 'cause, what if they've got hepatitis C"...

(Eilidh, 39, diagnosed 2013)

Such acts of passive and covert discrimination formed only a minor refrain within the analysis, because by their very nature, they are often unobserved and largely go unnoticed. The absence of such everyday acts of discrimination from the collected discourse speaks not of the absence of enacted stigma within society, but of the unconscious acceptance and routine nature of such prejudice, which makes it unmemorable, unexceptional and therefore rarely voiced.

5.4 Support

5.4.1 Family and friends

The emphasis on the psychological burden of HCV within the narratives produced a discourse which also highlighted the importance the participants placed on emotional support. The sources of this support were diverse, and particular to each participant's individual circumstances. However, where present, close family and friends were commonly positioned as central to preserving their emotional welfare, and regularly praised for their encouragement, reassurance and care:

...[HCV] takes a bit of your emotional energy away but, I've got so much support from, from my family, my kids, they were, they've been absolutely fantastic. They've been really really amazing about it. My daughter in particular went out and, she would, err, she would investigate everything that came back and gave me lots of positive support about what to expect.

(John, 54, diagnosed 2012)

5.4.2 Peer support

This broad and comforting support from family and friends could only go so far, and more HCV specific support from third sector agencies, support groups and peers was also frequently acknowledged and praised. Speaking to someone 'outside the family', who had personal experience of living with HCV, was particularly valued, and was repeatedly described as the first time many of the participants had started to learn more about their condition. Peer support and peer-led support groups allowed

participants to recount their experience within an environment that permitted them to let down their guard temporarily, safe amongst others who could personally relate to their experience:

D: ...but the groups an' everything that I went to, oh, they were amazing...

I: What do you get out of those?

D: Other people talking about what they go through erm, an' you're no' sort a' looked at as being different fae anybody else, where if you go to, like if I go to a nursery group, an' things are spoken about, I wouldn'ae turn 'round an' let parents at the nursery know exactly what I was going through, where people at [the HCV support group] I would.

(Danielle, 43, diagnosed 2009)

The importance placed on peer support was underscored by the wish some participants expressed to become involved in supporting others. A number of participants spoke of the immense value which peer support had contributed to their lives, and positioned repaying that support, and using their own experience to benefit others, as a natural and obvious step in their HCV journey:

I'm gonna start using my experiences maybe to try an' help people wi' hep C an HIV. If they want a' talk about it 'cause I've been through that experience – how am I coping wi' it? I mean even though sometimes I'm no coping wi' it, that's good an' all because people...it's jus' normal, y'know what I mean?

(Keith, 54, diagnosed 2004)

Peer support has previously been recognised as an important factor in the facilitation of access to HCV services for populations that may experience significant barriers to accessing care (Crawford and Bath, 2013). The ETHOS project in Australia has repeatedly demonstrated how peer support workers within opioid substitution clinics perform a valuable role in reducing barriers to HCV care, and how these workers are regarded as highly credible and trustworthy by those they support (Keats *et al*, 2015; Treloar *et al*, 2015). Peer support has been cited as one of ten priorities for expanding access to HCV treatment amongst PWUD in low- and middle-income countries (Ford *et al*, 2015), and the prominence of peer support amongst the participants' narratives in

this study suggests its value also extends to other more traditional care settings in high-income nations. Whilst family and friends were valuable sources of general comfort and reassurance, most participants placed a greater emphasis on support from individuals who had been through, or were going through, the same experience.

Whilst the participants' narratives predominantly framed their peers as valuable and beneficial sources of support, not everyone subscribed to this discourse, and atypical cases did exist. For Dean, who did not identify as a person who uses drugs, and vehemently positioned himself apart from those who did, the idea of speaking to others with HCV provided little comfort:

D: Groups?! What do the groups do? What, what do they hope to do, what do they hope to achieve? [pauses] Would I be in groups? Groups of what? People with hep C? [laughs] – so, you've got hep C? Err, yeah – you have? Err, yeah. So what do we do now?! [laughs]

I: So, you don't see any value in...

D: Not really no, no, to be honest. I mean, if there is a value in it, by all means, whoever can see that and get off on, get off on it or whatever, use it, put it to use, then by all means, indulge! But, I can't see any err, any, I can't see any kind of erm, anything I'd get out of it, any positive.

(Dean, 54, diagnosed 1997)

Dean's disparaging view emphasises that one size does not fit all. He mocks the idea that a group of HCV positive individuals could achieve anything together, and contests the notion of peer support being of value, framing it as a fix for those who indulge in the experience of being HCV positive. Whilst not as explicit, a more subdued endorsement of peer support was also located within the narratives of other participants who did not identify as PWUD, in comparison to those who did.

5.5 Discussion

5.5.1 Theme summation

By juxtaposing how participants framed the physical and emotional aspects of living with HCV, this chapter has aimed to illustrate how the burden of illness went beyond the physical manifestation of symptoms. Examination of the sporadic and inconsistent

accounts of the physical impact of HCV, contrasts with the pervasive and inescapable psychological and emotional burden produced by the participants' narratives. The burden of illness was multi-faceted. However, the exploration of stigma has illustrated how this enduring motif remained a key component of HCV's emotional toll, and continues to hold a stubborn and commanding grip on the experience of living with the virus. Due to the emotional burden of infection, the importance of support from friends, family and peers was repeatedly emphasised.

5.5.2 Addressing stigma

Stigma associated with HCV was an expected refrain within this study. Whilst the exposition of stigma within this chapter may not break new ground, the continued presence of significant tracts of analysis on the topic in contemporary HCV research stresses the influence it continues to exert on the lived experience of people infected with the virus. It exposes stigma as an immobile and obstinate presence, which has doggedly endured the dawn of a new era in the treatment of HCV, and remained untouched by the growing authority of HCV as a public health priority. The findings from this study are inconsistent with arguments that the stigma associated with 'long-term' conditions may be diminishing in light of technological and cultural changes in contemporary society (Green, 2009), and maintains stigma as a central and enduring motif of HCV infection.

Hepatitis C-related stigma continues to incite anxiety, shame and fear in those infected, contributing to detrimental outcomes in terms of both physical and mental health, and HRQoL (Miller *et al*, 2012; Treloar, Rance and Backmund, 2013). In addition, the persistence of stigma also has wider public health implications, as an adverse impact on the prevention of transmission, testing and diagnosis, access to treatment, and treatment adherence have also been repeatedly described (Harris, Ward and Gore, 2016; Hopwood, Treloar and Bryant, 2006; Miller *et al*, 2012; Treloar *et al*, 2013). Addressing HCV-related stigma therefore remains an important and vital part of the global response to the disease, yet governmental strategies for tackling this stigma, in conjunction with improving treatment outcomes, are poorly defined. Whilst there is a growing body of literature on how specific models of care can help reduce HCV stigma in a healthcare setting (Treloar *et al*, 2013), there is an absence of reports

evaluating population-level interventions aimed at addressing societal stigma more broadly. For example, even though the Scottish *Sexual Health and Blood Borne Virus Framework 2015-2020* (Scottish Government, 2015a) positions stigma reduction as one of its five major goals, strategies to reduce stigma are discussed in relation to HIV and sexual health, with no mention of strategies to address HCV-related stigma. This is despite evidence suggesting a range of interventions aimed at reducing the stigma of substance use disorders (of which, given its intimate association with injecting drug use, HCV could be considered comparable) have achieved meaningful results (Livingston, Milne, Fang and Amari, 2012).

Developments in drug therapy heralding a new era in the treatment of HCV may fail to reach their full potential without concurrently addressing the tenacious influence that stigma continues to exert on the lived experience of those infected.

Chapter 6

Reconstructing uncertainty

6.1 Introduction

6.1.1 Chapter aim

The aim of this chapter is to explore how the concept of uncertainty was fundamental to the inter-subjective experience of living with HCV. Uncertainty proved a persistent and compelling theme throughout the analysis, underpinning the participants' discourse and evident within multiple narrative threads. Uncertainty was present in the way participants spoke about the virus itself; in their understandings of how HCV had been acquired; and in their reflections on the effects of HCV to their health. Whilst these findings are briefly discussed, it is consideration of the nature of uncertainty around HCV treatment which provides novel and fresh insight into this much reported concept, and it is therefore this facet of uncertainty which constitutes the main focus of exploration.

By exploring the discourse surrounding HCV treatment, the main body of this chapter considers how interferon-based treatments were portrayed with conviction and assurance as an arduous undertaking, positioning a gruelling period of therapy as an unqualified certainty. It then contrasts this with the participants' narratives concerning interferon-free regimens, and unpicks the antecedents which have contributed to growing uncertainty around these novel therapies: the paucity of first-hand experience; confusion regarding multiple treatment options; and perceptions that the drugs are relatively untested. These insights are discussed in light of Mishel's theory of uncertainty in illness, which explores how this uncertainty was appraised as desirable and necessary, and considers the strategies participants employed to maintain this preferable ambiguity.

This chapter suggests that participants' understandings of HCV treatment have transitioned from certainty to uncertainty, a narrative at odds with the predominant medical discourse of an uncertain interferon-based era being replaced by the certainty of new, more efficacious, therapeutic regimens.

6.1.2 Uncertainty in illness theory

Uncertainty in illness has been defined as the inability to determine the meaning of illness-related events (Mishel, 1988). The concept of uncertainty in illness is widely recognised and reported, and a number of theoretical perspectives have been utilised to gain insight into the phenomenon (Han, Klein and Arora, 2011). Mishel's theory of uncertainty in illness concentrates exclusively on uncertainty experienced by patients, and, as such, resonates with the focus of this thesis. The theory originally focused on uncertainty in acute phases of illness (Mishel, 1988), but was later reconceptualised to include the experience of living with the continual uncertainty found within chronic conditions (Mishel, 1990). It is composed of three main themes: antecedents of uncertainty; appraisal of uncertainty and coping with uncertainty. The theory proposes that uncertainty exists in illness situations that are characterised by four key factors: ambiguity, complexity, unpredictability and inconsistency. It further proposes that uncertainty can be reorganised over time (Mishel, 1988; Mishel, 1990). The uncertainty in illness theory has previously been employed to gain insight into the lived experience of a number of other conditions, including fibromyalgia, multiple sclerosis and HIV (Brashers *et al*, 2003; Johnson, Zautra and Davis, 2006; Mullins *et al*, 2001), and provides a compelling foundation for the examination of understandings and insights gained in this chapter.

6.2 The antecedents of uncertainty in HCV

6.2.1 Uncertainty at diagnosis

A discourse of uncertainty was etched throughout the collected narratives, often established during discussion of how HCV was understood at the time of diagnosis. For many, HCV was a complete unknown, with participants commonly producing accounts of their diagnosis which emphasised their lack of familiarity with the infection, and stressed the uncertainty they felt at the time. The virus was an enigma, only vaguely comprehended and poorly understood. Associations were made with HIV/AIDS and other viral hepatitis, which raised questions and nurtured doubts in their minds:

...and [my GP] was like, can you sit down, an' I'm like I'm just in a' get my prescription, I'm in an' oot, an' she was like no I need a' speak to you, an' I

didn't even know what hepatitis C was, I was like, is this like HIV, is this gonna kill me?

(Fiona, 40, diagnosed 2012)

Further ambiguities and worries persisted: could friends and family have contracted HCV from shared plates, cups and cutlery? Could partners become infected through sexual contact? Could pets become infected? The lack of familiarity with HCV meant that participants possessed insufficient cues to structure or adequately categorise the diagnosis, and encountered difficulty when constructing a cognitive schema to make sense of it (Mishel, 1988). Additional antecedents such as the inconsistency of physical symptoms (described in chapter 5) contributed to the uncertainty, reinforcing a vague interpretation and ambiguous understanding of the meaning of their diagnosis.

6.2.2 Uncertainty of acquisition

Uncertainty was not limited to retrospective reflections on diagnosis, but pervaded and persisted throughout the collected narratives and across the illness trajectory. For participants who disclosed no history of injecting drug use, uncertainty was evident in the confusion frequently voiced as to the origin of their infection. Potential sources of contagion were often visited and revisited spontaneously by participants as the interviews progressed, with the uncertainty of when and how they had acquired HCV vehemently emphasised. This may have served as a discursive strategy, aimed at producing a persona which did not align with typical representations of individuals with HCV. However, the passion which often accompanied the words and the unprompted re-examination of the topic time and again suggested a deeper and more profound significance to their illness experience. The uncertainty of not knowing how it began, created difficulties in accepting the diagnosis and moving forward:

...and to be honest, I don't, I don't know how I caught it, I, I'd like to be trying a' get an explanation a' how I got it, err, they don't know if it was through the blood transfusion or not, I don't know, an' but, I've never had an explanation (...) I'm not, I'm not saying, not saying that I'm stupid but I don't, I jus' can't get my head round to why, why I've got it, y'know, because I don't know, an' that really does frighten me a bit as well, I'd like, if I could get an explanation. It makes it harder to accept it. All I'm wanting is to try an' get an explanation to why, because I'm, say I've never used anything in my life, y'know...

(Jacqueline, 70, diagnosed 1991)

6.2.3 The effects of HCV

In addition to uncertainty in the past, concerns surrounding the future progression of liver disease were frequently alluded to and/or explicitly focused on by the participants. Disease advancement was constructed as a pervading and preoccupying concern, particularly amongst those who had been diagnosed the longest. The discourse demonstrated confusion about the rate of liver disease progression, and whether advancing liver disease would display corporeal signs:

...you don't know how it could progress, it could, is it changing? How fast is progressing? Even though the appointments are six months apart what's happening in between? You think well, because I'm post-menopause, things could change an', oh, will I know about it?

(Marilyn, 52, diagnosed 1997)

These concerns resulted in participants seeking reassurance, and attempting to manage their uncertainty through interaction with healthcare services and seeking social support. Such actions provided structure and cues to aid the development of a cognitive schema to interpret and provide meaning to their illness experience, and ultimately reduce the uncertainty they felt (Hummel, 2016):

I think I'll be OK but I don't know what to look for if I'm not OK, so err, it's a matter of if I'm needing a test done, I'll get a test done.

(Sheila, 59, diagnosed 1991)

Uncertainty in relation to HCV disease progression has been described previously, with studies focused on individuals who were undergoing watchful waiting. Watchful waiting is a management strategy which defers treatment for those with mild- or moderate-liver disease in favour of monitoring by healthcare professionals, and was particularly prevalent prior to the arrival of DAAs due to the poor efficacy of the drugs available at the time (Colagreco *et al*, 2014). These studies emphasised the physical and emotional impact that illness uncertainty had on overall health, detailing associations with fatigue and depression which in turn negatively affected HRQoL (Bailey *et al*, 2009; Bailey *et al*, 2010; Colagreco *et al*, 2014). Watchful waiting remains a relevant strategy for patient management, as the high costs of interferon-free

therapies have led to treatment rationing (Wolfe *et al*, 2015). For Peter, the option of living with the uncertainty of disease progression whilst awaiting access to new therapies, or facing an interferon-based regimen was a no-win situation:

...the doctor said, we can maybe wait one year or two and see you every six months, so don't worry about it. An' I was worried at that point, because I jus' say to the doctor, err, I jus' want to start. I cannot keep that in the back of my mind (...) I thought can I live with that for a year on my mind, or do I go through hell an' take the interferon?

(Peter, 51, diagnosed 2015)

6.2.4 A familiar refrain

The discourse of uncertainty formed a compelling theme within the narratives, which resonated with previous published works. In a review of how HCV was socially produced amongst PWID, Rhodes and Treloar (2008) described uncertainty in relation to a number of factors, including understandings of transmission routes and the meaning of blood tests. Conrad *et al* (2006) reported uncertainty associated with the emergence of new symptoms in relation to HCV, and the lack of effective management strategies to deal with them. More recently, a phenomenological study from the UK described a multitude of antecedents of uncertainty including a lack of practical advice, information and support in people's daily lives, in addition to the uncertainty of disease progression and plans for the future (Hill *et al*, 2015).

Whilst the significance of uncertainty to the participants' experience of HCV within this study is a central theme, it is not a surprising one. The insidious nature of uncertainty has long been described as an inherent component of chronic illness (Hummel, 2016), and, as this brief discussion has shown, previous research focused on HCV, in addition to numerous other conditions, has repeatedly emphasised uncertainty as a key aspect of the lived experience (Brashers *et al*, 2003; Conrad *et al*, 2006; Hill *et al*, 2015; Johnson *et al*, 2006; Mullins *et al*, 2001; Rhodes and Treloar, 2008). The finding is evidently nothing new. Where fresh and novel insight can be found, however, is by the exploration of uncertainty within the context of HCV treatment. By first exploring the dogged embrace that interferon exerted, and continues to exert, over understandings of HCV treatment, a discourse of *certainty* can be traced, albeit a

certainty of suffering and misery. By then focusing on understandings of newer therapies, a transition from certainty to uncertainty in the inter-subjective understanding of HCV treatment becomes apparent, at odds with the certainty surrounding interferon-free therapies demonstrated within the medical discourse.

6.3 The certainty of interferon

The tenacious hold that interferon³³ exerted over the participants' narratives emphasised how the drug continued to influence the experience of being HCV positive in an age of interferon-free therapies. Chapter seven will examine how this interferon legacy was fundamental to the experience of participants taking interferon-free

³³ Interferons are categorised as glycoproteins, with their name deriving from their ability to 'interfere' with viral replication within a host cell (Kemp and Roberts, 2012). Their identification was reported in 1957 (Isaacs and Lindenmann, 1957), and they first came to public attention one year later with press reports branding them as potential 'antiviral penicillin' (Pieters, 2005). Interferons were framed as a magic bullet for viral disease, however early hopes failed to be realised and they soon returned to relative obscurity. As laboratory technologies and understandings of these drugs advanced during the 1970s, interferons were trialled in the treatment of hepatitis B (Greenberg *et al*, 1976) and multiple sclerosis (Jacobs, O'Malley, Freeman, Murawski and Ekes, 1982) with encouraging results. However, it was their possible clinical use in the treatment of human tumours which really revived their fortunes. Interferons were reframed as potential anti-cancer drugs within public and scientific discourse, leading to widespread optimism that a general cure for cancer may be within reach (Friedman, 2008). Global public expectation of these 'wonder drugs' was high, fuelled by media reports which eulogised their scarce and costly nature, christened them as 'weapons', 'miracles' and 'natural wonders', and likened them to 'God's own elixir' (Pieters, 2004). However, once again, such mounting hopes failed to be realised. In the early 1980s, the euphoria around a cancer panacea foundered on the back of uninspiring results from clinical trials, and interferons faded from public discourse once more (Pieters, 2005).

Although discouraging, this period of research into the interferons' anti-cancer properties had not been in vain. Interest in their potential as a cancer cure-all had led directly to the cloning of genes for human interferon- α (Nagata *et al*, 1980), which in turn led to the production of quantities of interferon- α suitable for use in clinical trials (Friedman, 2008). Clarification of the potential uses of interferons in treating human disease followed steadily, and their third incarnation as the most effective treatment against HCV took shape.

The use of interferon in the treatment of HCV predates the identification of the virus itself with early work focused on its activity against non-A, non-B hepatitis (Hoofnagle *et al*, 1986). Following the identification of HCV in 1989 (Choo *et al*, 1989), interferon monotherapy emerged as the most effective treatment option available (Poynard, 2004), and the drug remained a backbone of HCV therapy throughout the 1990s, 2000s and into the early part of this decade. Its name has been synonymous with HCV treatment for over 25 years, and has treated a generation of HCV positive individuals whose experiences have contributed to a growing notoriety and folklore. Details of treatment-related distress and a general deterioration in health-related quality of life have been consistently recounted in the scientific literature throughout this period (chapter 2). In addition, woeful SVR rates from interferon-based therapy conflicted sharply with its previous construction as a miracle cure-all (Fried *et al*, 2002), and its historical association with cancer and chemotherapy emphasised its toxicity and positioned it as a drug to be avoided. A combination of these factors led to interferon-free regimens becoming touted within the scientific and popular press as the ultimate goal of HCV treatment (e.g. Sulkowski, 2011) reinforcing the social understanding that interferon was a damaging, dangerous and harmful medication. This construction of interferon has proved a potent and compelling force.

treatments. Yet, it was the manner in which this notorious therapy was framed by the participants which provides meaning here. Although a demanding and onerous period of treatment was commonly discussed, it was done so with confidence, conviction and certainty.

6.3.1 An arduous certainty

For a number of participants, the initial impressions formed about HCV treatment were vague and ill-defined, gathered from various ‘horror stories’, and picking up information ‘on the grapevine’ or through ‘Chinese whispers’. Whilst ambiguous in nature, these notions of HCV treatment were unvaryingly negative, recounting a difficult and demanding course of therapy, which instilled fear and anxiety in the listener. The ethereal nature of where and how this knowledge was gained within the narratives speaks of its ubiquity within the social consciousness. There were often few specifics of the manner in which this understanding was acquired, more a general sense that this knowledge was somehow omnipresent, and absorbed without conscious effort:

J: Initially, it was just fear of the, the, fear of the medication because, you know, I had it in my head just-ju by, from what I could gather from, you know, without having done any research but I just had it in my head that the treatment for hep C at that point was gonna be really rough. That, that was the most, kind of, the most worrying thing.

I: And have you any idea where you’d picked that...where that...?

J: I don’t know, just from hearsay I guess, from knowing something on, on the, some documentary on TV or, just subliminally absorbing this information from wherever you know?

(John, 54, diagnosed 2012)

The underlying perception of the gruelling and demanding nature of a course of HCV therapy pervaded participants’ constructions of treatment. The harrowing nature of therapy was spoken about in terms of being an absolute truth, despite participants often having little awareness of what was practically involved or the origin and veracity of the claims. The perception of an arduous treatment was widespread, and was

inherent in the way the majority of participants framed their understanding of what treatment demands. The reputation of interferon preceded itself:

I: Tell me what you know about treatment; you said earlier that you knew, at the time when you were diagnosed, you knew the treatment was 'hellish'...?

D: Yeah, quite severe. Erm, I mean, at that point, I didn't know, other than that it was severe I didn't know anything about it, I didn't know the names of the drugs or anything like that, I knew that, they could, basically what I'd been told is it would make you feel like you were in withdrawal.

(Dan, 27, diagnosed 2013)

I: What do you know about hep C treatment?

E: Err, that I jus'...all I know that it's maybe make you really no' well. Err...

I: OK, can you tell me anymore?

E: I can't tell you any more than that; that's no' meant a' be nice treatment! [laughs]

I: Do you know what treatment involves?

E: I don't, no.

(Eilidh, 39, diagnosed 2013)

The significance of HCV 'horror stories' to the participants' understandings of treatment emphasises the importance of storytelling as one of the foundations for communicating human experience (Haigh and Hardy, 2011). Oral histories and personal stories align with ideas of common sense, and appear appealingly authentic and engaging compared to abstract elitist rhetoric (Polletta, Chen, Gharrity Gardner and Motes, 2011). Discouraging stories and bleak anecdotes of interferon experience have persisted and flourished in the understanding of HCV treatment, creating a powerful and pervasive communal comprehension. Hepatitis C treatment was positioned with certainty as a demanding and challenging beast.

6.3.2 Confirmatory experience

Some participants had direct experience of treatment in the interferon era and therefore possessed a greater understanding of what that treatment comprised. For those who had been through a previous course of therapy, or who had witnessed friends and family going through treatment, their experiences served to confirm and validate these societal understandings of what HCV treatment was assumed to be like. The 'horror stories' were not apocryphal tales, but rather experiential histories. The participants who had been through a previous course of interferon-based therapy described many of the familiar side-effects such as depression, weight-loss, fatigue and rashes commonly found within the existing literature (Fraenkel *et al*, 2006; Hopwood and Treloar, 2005; Taylor-Young and Hildebrandt, 2009). They spoke in general terms about their period of treatment being 'a nightmare', 'hellish' and 'horrendous'. Dean's account of his previous therapy vividly captured the trauma and distress he had endured:

...I'll tell you exactly what happened about the fucking treatment. I work in [states occupation], right, so basically [describes working outside at height as a result of his occupation], so I started the treatment, it was sound at the start, nae problems, but then, the brain started t' bloody go, right, an' I was coming home, an' I was greet...crying, an' it were at nights an' every'hing else [pauses]. Three times, I did it, just about [mimes letting go whilst standing at height] – standing there, holding on, looking doon, an' saying "I've fucking had enough" – easy jus' let go, done, down, finished, wouldn't have to worry about anything else. That was enough, an' I swear this, and I'll tell you the truth, the amount a' times I come in like that situation, I just...the brain couldn'ae handle what was going on...

(Dean, 54, diagnosed 1997)

For those who had witnessed others taking the medication, the experience of watching people struggle through a course of interferon-based treatment did little to motivate them for their own period of therapy. The support provided to others was framed by a couple of participants as almost as exhausting as taking the treatment itself:

...my partner went through it, two years ago an' she was the worst advert for treatment ever, erm, she actually had like two nervous breakdowns, had to go to [a respite facility] an' things. And, I was due to start like six month after she had finished and, well, I needed to, sort a' take a step back for a wee while

'cause, it was actually draining, helping her through it was, took a lot out of me as well y'know.

(Paul, 37, diagnosed 2000)

I'd seen people who'd been on it as well, an' that kinda scared me, because they were just like, 'this is, this is killing me man, an', I've never been right since I started the, the, the interferon' and stuff and 'it's really knocking me for six'. I thought, 'oh no' [makes scared groan], obviously worrying at times...

(Gary, 38, diagnosed 2013)

Perhaps unsurprisingly, this pervasive awareness of an arduous treatment had profound implications for the decisions participants made in relation to accessing HCV therapies. Many of the participants related accounts of having deferred taking treatment in the past due to concerns about interferon-related side-effects, and described being content to wait for alternate options rather than putting themselves through this difficult, but often little understood, therapy. Some recounted feelings of fear and terror at the thought of being prescribed HCV treatment and the impact this would have on their lives.

A: *Oh my God, oh...I was sort a' like, oh my God, y'know, I, I don't want a' do it, I don't want a' do it. Erm, I was, I was actually making myself really ill with the thought of, y'know, oh my God, I may be put on this stuff an' I may be ill an' all that an' err, nah, it was, I was like, nah, I really jus'...*

I: *Would you have rather not had the treatment than go through it?*

A: *Yeah, 'cause I was that, I was that petrified of, y'know, because, you're jus' going to be, ill, an' jus' basically probably housebound or whatever or, y'know, I, I jus' couldn't handle that thing, where y'know, you, you were going to feel like crap.*

(Anita, 46, diagnosed 2014)

Whilst most participants' narratives subsequently embraced, to a greater or lesser extent, the arrival of new therapies, the reaction of Eilidh, an injecting drug user on a daily methadone prescription and who had not engaged with HCV treatment services, is noteworthy. It exemplifies the tenacity of interferon folklore in the absence of any

tempering influences, and also highlights the impact this has on the lowly placement of HCV treatment within a life of competing priorities:

I: You've heard that treatment's terrible [E: um-hm], so – is that, has that affected you, from the point of view of you thinking about treatment?

E: Aye, 'cause it's almost put me off, it's almost putting me off want a' go for it. 'Cause I stay on my own...

I: Almost...?

E: Almost – I know that I'm gonna have to have it, to, to get better, but because I stay on my own an' I dunnae have like a...a network around me – I'm on a daily prescription so, if I'm no' well I'm gonna have to try t' drag myself oot a' my bed along a' that chemist a' get my script, an' the last thing you want a' do, when you're no' well – floored – is, go oot galavanting for a fucking prescription.

(Eilidh, 39, diagnosed 2013)

This experientially-based and pervasive understanding of an arduous treatment for HCV has been produced and reinforced over more than 25 years of interferon-based therapy. Individual experiences of treatment interweave with second-hand accounts of witnessing others on therapy, and are shared and passed on through friends, families, support networks and treatment services themselves, producing a version of HCV treatment which is tough and unrelenting, and giving rise to the 'horror stories' which in turn bolster the interferon folklore. Whilst it is recognised within healthcare settings that not all individuals experience such a hard time on interferon treatment, almost all the participants related only negative perceptions and experiences of the drug, which highlights the dominating role these accounts play in the social inter-subjective understandings of HCV therapy. The account of Marilyn, an HCV positive woman who had also performed some support work for others with HCV, demonstrates the partiality of bad experiences being discussed over the experiences of those who may not have encountered as many problems:

I: Do you know people who've been through hep C treatment? [M: Yes] Tell me what you've heard...

M: I've had people phoning me, depression phone calls, worse thing they've ever done, wish they hadn't done treatment, erm, it's ruined their life, they're not clear, depression, people crying, greeting on me, crying their eyes out, erm...an' then I've other people saying that's alright, I've had the whole spectrum. I've had people suicidal on it, all their benefits been stopped, telling sort my benefits out, can't get back to work, I've had other people's been fine. But I suppose you're gonna hear the worst of things, an' the people who're benefits have stopped rather than the good luck stories...

(Marilyn, 52, diagnosed 1997)

The data generated in this study reveal a hard-wearing societal understanding of interferon-based HCV treatment as an arduous and gruelling ordeal. Significantly, this idea of HCV treatment was spoken about with absolute conviction. The participants were definite and unambiguous in the way they constructed this recurring narrative. Interferon-based treatment was framed as an unpleasant and punishing regimen with certainty and confidence. In contrast, the discourse around new therapies emphasised uncertainty and ambiguity, as will now be explored.

6.4 The uncertainty of interferon-free therapies

6.4.1 A nebulous grasp

For those participants who had engaged with HCV services, the discourse surrounding new treatments for HCV revealed a range of understandings about what these therapies might entail³⁴. However, a common feature of all these notions and projections was a prevailing impression of uncertainty and confusion. Accounts of new treatment options were vague and superficial with declarations of complete ignorance not uncommon:

I: And what is the treatment?

S: I have no idea! Probably another pill to throw in a box, I have no idea what the treatment is.

(Sheila, 59, diagnosed 1991)

³⁴ For Eilidh, the one participant who had never engaged with secondary care, the discourse surrounding new treatments for HCV was absent from her narrative entirely.

I: *So if I asked you specifically what is the treatment now? [C: yeah] what would you say?*

C: *Tell me! [laughs]*

(Callum, 52, diagnosed 1995)

In addition to the nebulous grasp of emerging therapies demonstrated within the discourse, the narratives also exposed a seam of distortions and misinformation that a number of participants presented as factually accurate: the drugs had fewer side-effects but didn't work any better; the tablets would help, but not cure, the disease; pills would need to be taken at least every three hours. Such misrepresentations of new treatments had been assimilated from hearsay and anecdotes told by friends and peers, illustrating the continued importance of storytelling to the communication of experience (Haigh and Hardy, 2011). These inaccuracies also echoed the confusion which resonated throughout the testimonies around the plethora of new regimens becoming available. Counsel should be cautiously sought:

This is what...so it's hearing from other people, I mean it's good to talk to other people who've got the virus, but at the same time, you got a'...had to realise that there's all different treatments an' different stages...

(Stewart, 52, diagnosed 2015)

...there was jus' a lot a' misinformation about what treatment drugs people were on, whether it be first, the first treatment that came out, or the second one, or the newer one, because they're coming out so fast...

(Gary, 38, diagnosed 2013)

The provision of written information by healthcare staff on the practicalities of taking the drugs did little to challenge the confusion and uncertainty. The specifics of what, how many, and how often were framed as trifling concerns, with questions regarding side-effects and the treatment experience positioned as more significant but less addressed anxieties. Despite having literature on how to take his drugs, Phil still felt he knew nothing about them:

I, I know nothing about this stuff, all I know is err, I've been err, described on, how to take it, err, erm, an' how many times to take it, y'know, dosage, erm,

frequency of dosage an' all that, all that bumf, or whatever you wanna call it. Err...it, it is, it's all in here [refers to drug booklet] look - what is [names drug], what does it look like, what does it, err, do...an' all that err, stuff.

(Phil, 60, diagnosed 1997)

These insights are curious given the majority of interviews were conducted with the participants at the hospital outpatient clinic, often following an appointment with an HCV specialist specifically to discuss their potential treatment. However, research in other areas has reported the amount of information correctly recalled by patients following discussion with medical professionals is strikingly small (Kessels, 2003; van der Meulen, Jansen, van Dulmen, Bensing and van Weert, 2008). Therefore, the uncertainty and vague comprehension around new HCV therapies is unsurprising. Of note, level of education has often been cited as an important sociodemographic determinant of recall (Selic, Svab, Repolusk and Gucek, 2011; Watson and McKinstry, 2009). Although this was not recorded in the demographics for this study, the link between drug use and poor educational attainment has been well made previously (Fothergill *et al*, 2008). Another possibility is that participants actively avoided learning more about these new therapies for reasons which will be discussed further in due course.

6.4.2 Suspicion and scepticism

Expressions of suspicion and scepticism about new HCV therapies were also made by a number of participants. These apprehensions about the drugs were tied to personal previous experience of both illicit and prescribed drug use, and also a prevailing perception that the medications were currently in development and 'on trial'. Despite acknowledging the reassuring and optimistic rhetoric coming from healthcare professionals, a discourse emerged which emphasised the importance of caution and experience over blind faith.

For example, a belief that individuals would respond differently to the drugs based on unspecified innate factors was repeatedly voiced. As such, a perception that nothing could be taken at face value persisted. This notion was found predominantly amongst the narratives of those currently using drugs, or those who had done so in the recent

past, suggesting expectations of new HCV therapies were shaped by personal experience of illicit drug use (Maisto, Galizio and Connors, 2011). The testimony of Phil, who injected heroin daily, revealed measured expectations of new HCV therapies in line with his considerable drug experience:

I'm not expecting anything, I, I wait for, for what's gonna happen. If it turns out to be err, something that affects me, 'cause everything affects everybody differently, everyone's different, every drug affects everybody differently as you know, err...it, it might be, I might be jus' one of these people err, these awkward, err buggers [chuckles] that err, that erm...it, it doesn't, err, agree with.

(Phil, 60, diagnosed 1997)

For those co-infected with HIV, the familiarity of antiretroviral medications also imbued their narratives with significant drug experience. Doubts around novel HCV drugs were discussed in relation to understandings of the HIV therapies they had been prescribed over the years. All HIV/HCV co-infected participants had extensive histories of various HAART regimens, and a cautionary rather than all-embracing tone was adopted when it came to HCV therapy. Suspicions were voiced in relation to the perceived lack of scientific knowledge of the new drugs, rooted in their experience of failed HIV regimens, and novel HIV therapies which had subsequently been found to produce unforeseen side-effects. Hepatitis C therapies would need to be monitored closely, and treatment expectations echoed their experience with HIV drugs:

I: What do you envisage that treatment to be?

S: [long pause] I think it would be a matter of me being in [the hospital] for a few days, to see that it's settling down ok, then let me out and come back an', y'know, just keep it, a good eye on me.

I: So similar to HIV meds?

S: Yeah, yes.

(Sheila, 59, diagnosed 1991)

During the study, the main recruitment site also hosted two phase III randomised controlled trials for new HCV drugs, for which a number of participants had been approached by members of their multidisciplinary team. An awareness of clinical trials

was therefore common amongst the participants, and often underpinned many aspects of their testimonies. Apprehensions and suspicions about new HCV therapies arose from their perceived status as ‘trial drugs’, and were founded on the uncertain and unknown nature of such medications.

I mean the other night there, although there's no' been...I don't think there's been any deaths through the treatment an' things like that, but, I still sat an' wrote [my child] a letter an' things like that jus' in case anything did go wrong. Jus' explaining to her that, this only happened because I was trying a' make things better for us an' things like that...

(Danielle, 43, diagnosed 2009)

This perception was not limited to only those drugs actually being used in clinical trials, but more commonly applied in blanket fashion to refer to *all* new HCV therapies which were available in the clinic. A couple of participants who were not considering taking part in clinical trials still referred to themselves as ‘guinea pigs’ when contemplating their potential course of treatment, emphasising the novelty and nascent nature of the regimens. For a number of participants, scepticism was evident surrounding how representative and trustworthy the results of clinical trials may be, illustrating the perception that despite being licensed, these drugs were still largely unknowns:

I ken they've obviously done clinical tests an' that, but, that's in a sort a' controlled environment, but when you're talking about people who're, normal people who're suffering from depression an' drug problems an' all a' that, y'know what I mean, that kind a' goes oot the window, that clinical test...

(Keith, 54, diagnosed 2004)

The wariness of participants in relation to medications framed as ‘trial drugs’ can be illuminated by consideration of their relatively untested nature, and the inherent risks the actual medications may pose (Cox and McGarry, 2003). However, a further narrative strand embedded within the existing literature also offers some insight. Mistrust of the pharmaceutical industry and the drug development process has previously been observed in studies focused on patient attitudes to medication use (Bezreh, Laws, Taubin, Rifkin and Wilson, 2012), and may have influenced the

participants' discourse here. Disgust at the high costs of the drugs, and denigration of pharmaceutical giants were familiar refrains within the data:

I think pharmaceutical companies should be shot! They should get down a place. It doesn't cost that much to make, it's just them making money out of the hospital, playing with people's lives.

(Stewart, 52, diagnosed 2015)

6.4.3 Conflict

The uncertainty around access to new therapies, and the contemporaneous use of interferon-based regimens alongside interferon-free options created a sense of conflict for the participants. Whilst new, less onerous therapies were available, the chances of accessing these drugs in the immediate future were often deemed to be slim due to the need to fit stringent criteria. Decisions about HCV treatment were therefore framed as a trade-off: living with the virus and waiting indefinitely for access to improved therapies, or taking an interferon-based option:

[if the doctor] says there's a chance we could give you this new treatment, but you'll have to wait two years or three years, then I would wait you know, but if they say no that's not going to happen, then I would just have to deal with it and get on with [the interferon]...

(Kelly, 34, diagnosed 2008)

Whilst some participants eschewed the interferon option, in favour of an uncertain wait, others embraced whatever treatment regimen was offered. This latter approach was underpinned by the protracted and challenging journeys to treatment which many participants described, and which created a sense that they had already waited long enough. Some participants spoke about the years they felt they had already wasted by not addressing the infection previously, and repeatedly voiced a desire to 'just get on with it'³⁵. For others, a prevailing sense of wanting to be free of HCV at any cost developed, and a willingness to accept the ordeal and disruption of interferon-based regimens pervaded:

I mean, the end game is, erm, I want to go through the treatment, if, if it has to be a six month one that'll have to be, I mean I'll, have to grin and bear it eh?

(Paul, 37, diagnosed 2000)

³⁵ Gary, 38, diagnosed 2013

Because I feel like I have a, a, a time bomb inside my body, that it can trigger any, any minute (...) I'd rather take the twenty-four injections now, all at once! Another box!

(Peter, 51, diagnosed 2015)

This discourse echoes the acceptance of health inequalities and lack of entitlement that disenfranchised HCV communities have become acclimatized to, previously discussed in chapter four³⁶ (Wolfe *et al*, 2015). The readiness to accept an inferior treatment in an age of interferon-free therapies positioned the participants as submissive recipients of healthcare, rather than active and emboldened consumers, emphasising weak and undeserving notions of therapeutic citizenship (Rhodes *et al*, 2013). Within an age of improving therapy, the experience of seeking treatment for HCV constructed in the narratives was one of passivity and deference, to both medical authority and economic restraints.

6.5 Discussion

6.5.1 A return to theory: appraisal and coping with uncertainty

A discourse of uncertainty was woven throughout the participants' narratives of new HCV therapies. The multiplicity of available regimens, the perception of their new and 'untested' nature, and the doubts around being able to access the drugs all contributed to the construction of new HCV treatments as ambiguous unknowns, often met with wariness and apprehension. However, this exploration of the antecedents of uncertainty gives only partial insight into the concept, as it is how uncertainty is subsequently appraised and coped with that provide Mishel's theory of uncertainty in illness with its second and third key themes.

Mishel (1988; 1990) proposed that uncertainty is neutral until it is appraised as either a danger or an opportunity, with such appraisals established on individual attitudes, beliefs and personality dispositions. She suggested that the appraisal of uncertainty as an opportunity would occur when the alternative is a negative certainty, or where not knowing is better than knowing (Greenwood, Mackenzie, Wilson and Cloud, 2009). Whilst this aspect of the theory has not been applied to advances in drug therapy

³⁶ Section 4.3.2

before, it resonates with the findings discussed in this chapter. Interferon-based treatment was unequivocally constructed as a negative certainty: it would be a gruelling, protracted and toxic endeavour, which placed newer therapies as uncertain opportunities. The uncertainty ascribed to interferon-free treatments was preferable to the certainty of a negative experience with interferon-based regimens for the majority of participants. The uncertainty was a *desirable* uncertainty, as were it to disappear, the belief in a positive treatment experience could be destroyed (Mishel, 1988). The maintenance of uncertainty served as a coping strategy, preserving hope for the future (Hummel, 2016).

Maintaining this preferable uncertainty required buffering strategies aimed at blocking additional information which may have served to challenge the uncertain status quo (Baldwin, 2005). Buffering strategies include evasion and selective ignoring (Mishel, 1988), which sheds new light on previous discussion of how participants expressed poor information recall and limited understanding of new therapies. By actively avoiding further information regarding new HCV treatments and producing a narrative which emphasised unfamiliarity and ignorance, the participants circumvented any challenges to their hopes for these drugs. Knowing less, or constructing a persona of knowing less, maintained the desirable uncertainties which had been constructed around these medications, and upheld their appraisal as opportunities. Similarly, by framing these treatments with scepticism and suspicion, uncertainty was preserved and sustained, allowing participants to maintain hope, or at least avoid having their hopes dashed, and adapt to this new era of therapy.

6.5.2 Theme summation

This chapter has focused on the primacy of uncertainty within the collected narratives. Whilst uncertainty has long been observed as an intrinsic feature of both chronic and acute illness, it is the exploration of uncertainty with regard to the evolving landscape of HCV therapy which provides relevant and novel insight here. The negative certainty with which a period of interferon-based therapy was constructed by the participants has transitioned to a desirably *uncertain* framing of interferon-free regimens. This uncertainty is maintained by information avoidance, suspicion and scepticism: strategies which work to sustain hope. Whilst this juxtaposition of scepticism and

hope may seem paradoxical, it underlines how uncertainty was framed as an opportunity within the narratives. Maintaining a protective veil of uncertainty (by being sceptical, suspicious and poorly informed) allowed the opportunity of new therapies to persist. This argument gains clarity if considered from a different perspective: if participants viewed these much vaunted drugs as guaranteed, cast-iron certainties, then any perceived challenges to that construction could destroy their hopes entirely. Uncertainty was therefore beneficial, protective and advantageous to the lived experience.

This narrative contrasts with the conviction and assurance which greets new HCV therapies in much of the medical literature. Interferon-free regimens have been framed as 'a triumph' (Pawlotsky *et al*, 2015a), with 'spectacular response rates' commonly eulogised (Chung and Baumert, 2014) supported by a 'robust evidence base' (Thiagarajan and Ryder, 2015). Note the discussion of pharmaceutical developments in chapter one. The disparity between the ubiquitous medical discourse of success, and the perception of a protective and desirable uncertainty found within this study is striking, and has implications for clinical consultations. Healthcare professionals' attempts to quell misgivings, dispel rumour and resolutely educate may not always produce the desired response in those infected with the virus.

Chapter 7

The lived experience of interferon-free treatments for hepatitis C

7.1 Introduction

Following their initial interviews, eight participants who subsequently completed a course of interferon-free HCV treatment were invited to meet with the researcher again for a further semi-structured interview more specifically focused on their treatment experience. These interviews were conducted at the hospital out-patient clinic which had prescribed their medication, and took place between September 2015 and March 2016. Four of the participants were interviewed on their final day of treatment, with the others meeting the researcher after routine follow-up clinic appointments between two to four weeks after the end of therapy. Whilst an interview schedule was used to structure the discussion (appendix C), the transcripts from the participants' initial interviews were also employed to revisit some of their specific pre-treatment expectations and beliefs.

The aim of this chapter is to present the thematic analysis of this treatment-related interview data, focusing on three overriding themes which encompassed the experience of interferon-free therapy³⁷. The themes are described and developed individually in order to structure and explore the intersubjective commonalities which unified the participants' narratives. However, it is only by considering how these themes converge and interact, and the similarities, tensions and discrepancies between them, that a richer and more complete insight into the lived experience of interferon-free HCV treatment can be expounded. The relationship between the three themes will therefore be examined.

The three themes which resulted from the thematic analysis of this interview data have been named 'expectations and realisations', 'an honour and a pleasure' and 'treatment needs'. The naming of these themes sprang directly from the immersive and iterative experience of analysis, and aim to encapsulate the insights and understandings gained (Braun and Clarke, 2006). The theme 'expectations and

³⁷ The findings from this chapter have been published separately, and are found in appendix A

realisations' describes the influence that interferon continued to cast over the interferon-free treatment experience, contrasting the practicalities of taking interferon-free therapy and its associated side-effects with preconceived notions. 'An honour and a pleasure' integrates the persuasively upbeat and optimistic discourse around taking interferon-free therapies which pervaded the narratives, with the concurrent feelings of guilt and luck which were also manifest within the participants' accounts. Finally, the theme of 'treatment needs' grew from the combination of two elements, the discourse concerning support, and the participants' approaches in their search for treatment efficacy.

7.1.1 The participants

Prior to examining these themes in more detail, it is necessary to provide some context to the individual participant testimonies. The eight interviewees were a purposefully diverse group, whose eventful journeys to HCV treatment and personal circumstances were often conspicuous in their narratives. As such, a brief precis of each participant's disclosed history and social circumstances provides some background context and perspective to their experience (table 4).

7.1.2 A shifting landscape

Whilst these participants all received interferon-free treatment for HCV, they did not all receive the same drug combination. During the study, national guidelines and local recommendations for the treatment of HCV with DAAs were revised and amended continuously, in response to economic considerations and emerging scientific evidence. For example, HIS and NHS National Services Scotland (2015b) published guidelines for the treatment of HCV in August 2015 recommending the combination pill *Harvoni*® as first line therapy for those with HCV genotype 1. Only four months later, these recommendations were revised to favour first line treatment with the combination drug *Viekirax*® and *Exviera*® (HIS and NHS National Services Scotland, 2015a) following a contract award by NHS National Procurement to the pharmaceutical company AbbVie in September 2015, worth over £20 million (Public Contracts Scotland, 2015).

Table 4: Biographical information on the eight participants who shared their experience of interferon-free HCV treatment.

| Participant | Biographical Profile |
|-------------|---|
| Danielle | 43-year-old female, diagnosed HCV positive in 2009 most likely from sharing injecting equipment. Intermittent history of engagement with HCV care since that time. Currently prescribed methadone following a long history of injecting drug use. Lives with her mother and youngest child. |
| Gary | 38-year-old male, diagnosed HCV positive in 2013, identifies injecting drug use as the cause. Currently receiving a methadone prescription, and disclosed regular cannabis use in addition. Lives with daughter and son-in-law, and describes himself as a voluntary worker. Relates concurrent anxiety and depression as on-going concerns, along with other physical comorbidities. |
| Happy | 51-year-old female, lives with her two children and grandchild. Reports a history of significant alcohol use, but despite having partners who were regular drug injectors, denies any use herself. Diagnosed in 2005, presumes infection is sexual in origin. Currently unemployed. |
| John | 54-year-old male, diagnosed in 2012. Reports a brief history of injecting drug use in the 1980s, and dates the infection from this time. Lives with his wife, and has a supportive wider family. Works full-time and has deferred HCV treatment in the past due to concerns over side-effects. |
| Keith | 54-year-old male, diagnosed in 2004. Has a long history of injecting drug use and extensive prison experience. Co-infected with HIV, is currently stable on HAART and receives a methadone prescription. Lives alone, unemployed, and describes depression as a significant co-morbidity. |
| Peter | 51-year-old male, diagnosed in 2015. Self-employed running his own business, and living with his long-term partner, the source of infection remains an unresolved issue. Reports no significant medical history or drug use, and is a social alcohol user. |
| Steve | 45-year-old male, diagnosed in 2005. Describes himself as being in recovery for the last three years following an extensive history of drug use. Has comorbid psychiatric diagnoses, is currently unemployed and lives alone. |
| Stewart | 52-year-old male, diagnosed in 2015, confused as to the origin of his infection. Comorbidities include anxiety and depression, however remains in full-time employment. No history of drug use reported, although alcohol use features regularly in his discourse. Lives alone, and has a long-term partner. |

This rapidly shifting landscape was further complicated by variations in treatment regimens which were governed by the degree of liver disease and specific HCV genotype of individual participants. In addition, the hospital out-patient clinic which prescribed the HCV therapy was also a centre for a number of phase III RCTs for

unlicensed DAAs, which were recruiting in tandem with this study from the same cohort of patients. Due to a combination of all these factors, variation existed between the interferon-free regimens which were prescribed, and further details of the four different regimens used amongst the eight participants are given in table 5. However, the primary focus of analysis within this chapter is not the variation between interferon-free treatments, but how HCV treatment is understood and experienced when it no longer includes the one drug, interferon, which has defined and characterised it for over 20 years. In order to protect participant anonymity, the specific treatment each individual received has not been specified. However, whether this treatment was a single or multi-tablet regimen has been noted alongside participant quotes, to illustrate how the themes described were common to all and not connected to specific therapies.

Table 5: Details of the four different HCV treatment regimens taken by participants.

| Treatment Regimen | Single- or Multi- Tablet Regimen | Number of Participants |
|---|-------------------------------------|---------------------------|
| Sofosbuvir/ledipasvir (<i>Harvoni</i> [®]): combination tablet taken once daily. Licensed for use within Scotland for the treatment of HCV genotype 1 and 4, and for restricted use in genotype 3 (Scottish Medicines Consortium [SMC], 2015a). | Single-Tablet | 4 |
| Ombitasvir/paritaprevir/ritonavir (<i>Viekirax</i> [®]) + dasabuvir (<i>Exviera</i> [®]) + ribavirin: a combination tablet taken once daily, in conjunction with two twice daily medications. Licensed within Scotland for the treatment of HCV genotype 1 (SMC, 2015b). | Multi-Tablet | 2 |
| Sofosbuvir (<i>Sovaldi</i> [®]) + daclatasvir (<i>Daklinza</i> [®]) + ribavirin: combination of two once daily tablets in conjunction with one twice daily medication. Licensed in Scotland for use in the treatment of patients with significant fibrosis or compensated cirrhosis in genotypes 1,3 and 4 (SMC, 2014). | Multi-Tablet | 1 |
| Glecaprevir + pibrentasvir: fixed dose combination with pangenotypic action, currently in phase III clinical trials. Not currently licensed for use in Scotland (UK Medicines Information, 2016) | Single-Tablet | 1 |

7.2 Theme: Expectations and realisations

7.2.1 Interferon's influence

Despite each participant receiving treatment for HCV with an interferon-free regimen, the discourse surrounding treatment expectations was permeated and entangled with societal understandings of interferon-based therapy. The manner in which participants spoke about interferon emphasized and reinforced the fiercely negative societal perception of this drug (see chapter 6) and accentuated its disconcerting and distressing aspects over any curative benefits it may have shown. The influence of the drug that defined and characterised HCV treatment for over 20 years was prominent within the narratives of the participants. 'Normal' life would surely be forfeit for the duration of their interferon-free therapy, and the potential cure would come at a short-term cost:

...I mean, if I spent three months of feeling a bit groggy, tired and miserable and I come out in the end of the [hesitates over next few words], with err, you know, with err, good err, blood, err then it's, you know, it's worth that sacrifice...

(John, 58, multi-tablet regimen)

...'cause I jus' said that to my daughter it must a' been about two-three days ago, I said it's bizarre, I said like, here I am, as I am, all, getting on wi' it, an' in three days time I start medication, erm, I could, look like I'm, I'm on death's door. I said, how bizarre is that, you know what I mean, when you think, that there's actually something wrong wi' me but you're aw'right, up until you take the medication and that's when, symptoms kick in.

(Gary, 38, multi-tablet regimen)

Common side-effects of interferon such as lethargy, depression and weight-loss were referenced explicitly as expectations for interferon-free treatment by a number of participants. These expectations were not just trivial speculation however, as participants discussed how practical preparations were made to forestall the impact of these perceived inevitabilities. For Stewart, the strength of his beliefs around the detrimental effect that HCV treatment would have on his physical and emotional wellbeing was demonstrated in the meticulous planning that accompanied his first dose of the drugs:

First tablet, left [the clinic], went home, sick bowel, towel, duvet, tissues, waiting for it to come on. (...) I prepared ready a' be sick, I'd, I'd sent my partner away in case I was, really ill, know, kind a', I don't want a' be sick or, or screaming at people. I, I, I thought I was gonna be agitated, angry...

(Stewart, 52, single-tablet regimen)

Interferon was styled as a powerful drug within the narratives, repeatedly referred to as 'strong' by a number of participants. This perception of pharmacological strength was maintained when conversation turned away from interferon and towards DAAs. Participants believed that drugs still needed to be potent and powerful in order to treat the disease, and this perceived strength of drug equated with the expectation of physiological collateral damage. The idea of 'no pain no gain' prevailed; an unpleasant, demanding and strenuous period of treatment must surely result from drugs formidable enough to eradicate such a virulent and persistent virus. The notion that effective treatment must be accompanied by toxicity and short-term suffering is not unique to HCV. The concept of 'no pain no gain' has long been discussed in the realms of oncology, where reports of cancer patients requesting more aggressive and noxious therapies in the belief that these equate with improved efficacy are intermittently found (Gradishar, 2015)³⁸. A recent qualitative study describes the delight of one participant with breast cancer whose hair began to fall out during chemotherapy (Trusson and Pilnick, 2016): due to a lack of side-effects she had been convinced her treatment was ineffective, however the onset of alopecia assuaged her doubts.

In line with the 'no pain no gain' mentality, a general pre-treatment strategy of 'prepare for the worst, hope for the best' prevailed amongst the participants. Although frequently reporting that they had been reassured by healthcare professionals about the lack of side-effects, accounts of preparing for the worst created a compelling and undeniable narrative within the data, with 'the worst' commonly framed in terms of interferon folklore. This strategy served as a mental safety-net for participants, safeguarding them against the optimistic expectations of

³⁸ This belief has some basis in the research literature; for example, the development of an acne-like skin rash during treatment for non-small cell lung cancer has been shown to be predictive of overall disease free survival (Liu *et al*, 2013). Similarly, women who experience hot flushes whilst treated with tamoxifen for early-stage breast cancer may be less likely to develop a recurrence (Mortimer *et al*, 2008).

treatment that healthcare staff advocated, but which clashed too greatly with their societal understanding of how HCV treatment would be:

I don't know how this is gonna affect me. I've prob'ly been, lookin' at it, 'cause it's jus' how I do is – worse-case scenario, this is gonna wipe me out, I'm gonna feel completely utterly terrible, hoping, well no hoping but if anything, if it's not as bad as that, then at least, I can balance it, it's jus' my, my thought process an' that's jus' kinda how I work things, I look at worse-case scenario an' if it's not that bad then, hey – that's a bonus to me as far as I'm concerned...

(Gary, 38, multi-tablet regimen)

Once treatment had started, a sense that participants continued to await the expected onslaught of side-effects persisted. Whilst mild symptoms and treatment-related ailments were acknowledged and dealt with, there remained a feeling that these were only a precursor or a prodrome for more significant and unmanageable complaints yet to come. Participants described a period of constant waiting, which was ultimately unwarranted:

...this tiredness is gonna trigger something, like vomiting, or really really being really exhausted or something; but it never really does.

(Happy, 51, single-tablet regimen)

The pervasive understanding of the experience of HCV treatment remains grounded in interferon folklore, shaping contemporary discourse around treatment expectations. This intersubjective understanding of HCV treatment as gruelling and arduous counters any assurances of minimal side-effects and an easier time on therapy, fundamentally mitigating their impact. The disparity between the social understanding of HCV treatment and the discourse from healthcare professionals around these new medications leads to individuals hoping for the best, but ultimately preparing for the worst.

For the majority of participants, the realisation of their worst fears and expectations did not materialise during their therapy³⁹. However, a discourse surrounding

³⁹ The exception to this was Gary, who presented a nonconforming case. This will be discussed in due course (section 7.5)

treatment side-effects did become evident as analysis of the post-treatment data progressed. Examination of these narratives revealed a generally mild and manageable experience, significantly removed from the imagined horrors of therapy which had been so vividly constructed.

7.2.2 Side-effects

A number of familiar physical side-effects recurred within the participants' accounts of their treatment experience. Headaches were described by the majority of participants, commonly depicted as occurring near the start of therapy and often framed as a sign that the body was adapting to the medication. The headaches ranged in severity, described as anything from transient and quickly resolving, to an intensity that had not previously been encountered:

Err, headaches are like, supposed to be a really common cause, but I've never experienced headaches like that, it's like migraines, an' err, I've had it similar before likes drinking energy juice a lot, an' then stopping it, an' that gives you a, a blinding headache, rights, an' that's what it reminded me of...

(Steve, 45, multi-tablet regimen)

Similarly, bouts of nausea were also fairly commonplace, particularly at the beginning of the treatment, with a lack of appetite and increased lethargy also denoted as episodic features of therapy. However, these physical complaints were rarely stressed or emphasised by the participants, more commonly mentioned in passing or casually alluded to as minor inconveniences. Descriptions of specific physical ailments were embedded within concurrent narratives of feeling well, and having little to complain about:

Erm, because physically I was fine, I cannae say there was anything really bad, the first two weeks, the headaches an' I got quite a lot a' bleeding noses, but then I jus' started sort a' taking painkillers for the headaches, then, when I came [to the clinic], I had quite a bit a' constipation, so they gave me something for that, but that was it, nothing else.

(Danielle, 43, single-tablet regimen)

Participants were able to manage their physical side-effects with little difficulty, relating strategies which encompassed both alleviative medications and adaptive behaviours. Daily routines were slightly altered, dietary intakes were adjusted and plans were temporarily put on hold. However, none of this was framed as particularly onerous or taxing. A couple of participants also hesitated to ascribe these general and non-specific complaints to the HCV treatment at all, noting other potential sources and explanations within their narrative:

I got two days of a very - I feel like I've been run by a bus, y'know, an' I thought, ahh, that must be the flu symptom they were talking about, an' I feel, an' I feel like no energy, none, two three o'clock in the afternoon I jus' want to go to bed, but, I don't know it was the tablet? Or, I got the, the flu jag before the start a' the treatment...

(Peter, 51, single-tablet regimen)

Whilst most of the physical side-effects within the narratives appeared routine, expected and reasonably innocuous, a couple of participants experienced side-effects which had not been anticipated. Stewart related his surprise at the effect his therapy had on his libido, but presented this as a temporary and manageable situation, and one that hadn't impacted on his relationship to any great extent:

...it's no' very good for your sex life (...) it's no', it's a, it's a passion killer havin' a' use fucking durex anyway like, it's like brewer's droop, that's the way, I mean, I'm going out for a freebie dinner tonight wi' [my partner], an' she's already jus' decided that one way or the other we're going away fae the weekend [laughs], so we do talk, y'know what I mean, it's no' like I'm saying oh you jus' lie on that bed I'll go a' that bed, so it's, we have a laugh about it as well of course...

(Stewart, 52, single-tablet regimen)

The removal of interferon from the HCV treatment regimen had not therefore removed the physical aspect of therapy from the equation. Somatic side-effects continued to be experienced, requiring action from the participants to address and manage them, but the overriding impression was not of dramatic disruption, but of minor inconvenience. The weight of importance placed on these physical ailments within the narratives was low, their significance often minimised by participants

comparing them to what they understood of interferon-based therapy, their own preconceived notions of treatment, and to challenging times in their own life when they had experienced much worse.

Physical side-effects were not the only ailments attributed to HCV treatment however. A number of participants also related accounts of psychogenic ill-health, which they resolutely ascribed to their HCV therapy. This discourse was predominantly situated within the narratives of participants who disclosed a history of mental illness pre-HCV treatment, and was virtually absent from those for whom mental health had never previously been a concern⁴⁰. A couple of participants described exhausting alterations in their mood, spontaneously fluctuating from happiness to dejection:

Well, I'd say, emotionally, it's very draining, one minute you can feel on top a' the world, an' then within half an hour, forty-five minutes, you're so depressed, everything jus' seems - hectic.

(Danielle, 43, single-tablet regimen)

Emotional side-effects were most commonly framed in terms of low mood and transient depression, and their detrimental impact on relations with family and friends were often emphasised. However, the psychological impact of interferon-free treatment wasn't limited to this, and for Steve, who reported multiple additional psychiatric diagnoses, a more debilitating experience emerged:

I struggle really bad daily now, I mean likes a', err, it's got that bad it's like, really bad. Don't know how it done it like, but erm, even when I'm at [the respite facility], I, I could sit there in, in my room, an' jus' have a full blown panic attack going wow, where did that come from? At home it's worse, y'know, err, it's terrible, it's absolutely terrible, y'know. Maybe it's the anxiety of the - I don't know, it could be anything, it could be anything, but, it's got worse since I took the tablets, ten times worse.

(Steve, 45, multi-tablet regimen)

⁴⁰ The exception to this was Happy, who had no history of mental illness but spoke generally of “feeling moody” during her interview. Happy was treated with an interferon-based regimen initially prior to being switched to an interferon-free course, and her narrative was somewhat ambiguous as to whether her emotional difficulties were experienced during the interferon-free period in addition to the interferon-based therapy.

After some brief reflection, Steve offered potential explanations for his emotional instability which encompassed more than the pharmacology of the treatment. He acknowledged that the physical act of having to take HCV therapy twice a day had brought it to the forefront of his mind, and positioned his future as contingent on the outcome. For Steve, a period of HCV treatment meant confronting a reality he had previously been able to put to one side, and this in itself generated anxiety and concern:

...it's got a lot to do wi' the mental side of it like, y'know, because you're really wanting this treatment a' work an' you're conscious of it 'cause you're taking the morning an' at night, you're conscious of always being on this treatment, so likes, when I wasn't I, I'd forget about it for months, I forgot all about I had hep C. Y'know what I mean?

(Steve, 45, multi-tablet regimen)

Similarly, Danielle's narrative positioned undertaking HCV treatment as an act which allowed increased scrutiny into other aspects of her life, creating additional strain and worry. She repeatedly related concerns about how others would appraise her ability to look after her child during therapy, magnifying the vulnerability she already felt as a 'drug-using mother'. These anxieties focused her to present a version of interferon-free HCV treatment where she coped and managed with ease, but the disparity between this and her actual experience generated significant stress:

I'm no' gonna say everything's perfect, because my housework an' things like that sort a' hit rock bottom an' that, 'cause I was exhausted, but, where [my child] was concerned, I knew I had to keep on top a' that or people would start, right, well we'll jus' get a social worker out to see how you're coping, so, I jus' pushed myself a' make sure it was done.

(Danielle, 43, single-tablet regimen)

The physical act of taking interferon-free HCV treatment, irrespective of the specific drug combination, appeared to exacerbate pre-existing mental illness in some participants. Anguish, depression and emotional strain during the treatment process grew from the importance participants placed on being cured of HCV, and from the increased scrutiny they felt a period of treatment placed them under. However, these

difficulties were still largely framed as being considerably less onerous than if prescribed an interferon-based therapy. For example, the account above appeared towards the end of Steve's narrative, almost as an afterthought or addendum. Earlier in his interview Steve had described his treatment as *"nowhere near as bad on your mental health as [interferon]"* and how he *"thought the medication was fantastic"*. The impact on mental health from interferon-free treatment was considered and framed in respect of the imagined greater influence that interferon-based therapy would have, and, as such, its significance was diminished and symptoms became manageable.

Whilst the discourse surrounding the experience of side-effects created an impression of largely unmet expectations, there were still aspects of interferon-free treatment which the participants framed as *more* problematic than they had anticipated, most notably the number of tablets they were required to take.

7.2.3 Practicalities

A number of factors relating to the practicalities of taking the medications became evident within the participants' narratives. These formed a further thread to the theme of expectations and realisations. Despite a preponderant impression of the side-effects of interferon-free therapy being comparatively innocuous, every participant noted that their experience had been shaped by other difficulties which they had encountered during the treatment period. The physical size of the tablets and the difficulty in swallowing them were emphasised by a number of participants. For those on multi-tablet regimens, a sense of being misled as to the simplicity of treatment became noticeable:

The, the biggest thing that I think, I find was erm, the fact when the new treatment came out it was, it sounded more like it was jus' like more or less a single or two single type a' tablets (...) even though the course was of three, four, five – ten different tablets that I was taking during the day anyway, so, I think that, that was the only thing that I was slightly sceptical in the way that that came across, but that's still a hell a' lot a' drugs to be packed into a small amount, an' it still is a hell a' lot smaller compared to...what the older treatments could a' been, so, I get that, but it is jus' the way it kinda sounds.

(Gary, 38, multi-tablet regimen)

The accounts of participants on multi-tablet regimens underscored how the therapy was not taken in isolation, but incorporated into a life which was often already crowded with complex polypharmacy. The HCV treatment was an addition to catalogues of pre-existing medications such as opioid substitution therapy, anti-psychotics, anxiolytics, antiretrovirals, analgesics and other over the counter remedies which constituted an existing everyday routine. In addition, adjuncts to HCV treatment to combat nausea, headaches and other side-effects were also added into this expanding pill burden:

Erm, but they, they're quite hard, hard to swallow, 'cause there's quite a lot 'a tablets, especially, and you've got to take your other tablets with them as well so you end up like taking a big pile of them...

(Steve, 45, multi-tablet regimen)

This discourse contrasts with the accepted assertions of low pill burden with interferon-free HCV treatments expounded in much of the published literature. For example, Lam, Jeffers, Younoszai, Fazel and Younossi (2015) and Coppola *et al* (2015) both explicitly cite low pill burden as one of the benefits of interferon-free treatment in the abstracts to their reviews of second-generation DAAs. However, they fail to contextualise or quantify this within the articles. The casual and nonchalant use of the phrase 'low pill burden' belies that it is not an absolute truth in relation to new HCV therapies, and for those on multi-tablet regimens within this study, pill burden remained a significant feature of their course of treatment. The importance of this narrative is evident when research from other medical fields is considered. For example, lower pill burden and reduced dosing complexity have been related to better adherence in studies focused on HIV antiretrovirals (Nachega *et al*, 2014), and in haemodialysis patients with end-stage kidney disease (Ghimire, Castelino, Lioufas, Peterson and Zaidi, 2015) amongst others. Similarly, recent qualitative work from India has described pill burden as an influencing factor in the high percentage of patients lost to follow-up whilst receiving treatment for multi-drug resistant TB (Deshmukh *et al*, 2015; Shringarpure *et al*, 2016). The significance of pill burden to treatment adherence and completion is well described within the scientific literature, emphasising the importance of policy-makers including patient experience of interferon-free HCV treatments in their decisions concerning first-line therapies.

Given the need to take these regimens consistently, routine and aides-memoire became important in structuring the course of treatment. Participants on both single- and multi-tablet regimens described using calendars and alarms to keep track of their adherence, as well as appending it to existing regimes:

I: How did you remember?

D: By setting my phone alarm. I missed it once, when I came my first time, erm, but I managed to work all that out after that, I made sure I had my alarm set at a certain time an' jus' took them.

I: And it fitted into your life?

D: Aye, it didn'ae sort a' bother me, I think because I jus' took them along when I was taking my methadone every morning...

(Danielle, 43, single-tablet regimen)

...remembering was alright because I knew I had to take them every day, an' I didn'ae want a' miss any, 'cause I didn'ae want a screw up, so that's why I was, I always remembered to take them, always made a point [repeats as a mantra] - tablet the night, tablet the night...

(Keith, 54, single-tablet regimen)

Despite these practises, reports of missed doses were still apparent. Some participants on multi-tablet regimens described becoming lackadaisical and forgetful as the treatment course progressed, or struggling to fit multi-daily dosing into their existing routine. Fears around the consequences of missing doses were discernible, however, adding to the anxiety previously described:

I didn't want a' miss any, any a' the pills, an' it's really easy a' do, y'know, err, it's not as if you can double-dunt them either, y'know, so it's like oh no, an' you're always nervous about likes, oh I'm suppose to take them regular, if you're missing a gap out here an' there what happens?

(Steve, 45, multi-tablet regimen)

7.2.4 Theme summation

The 'expectations and realisations' theme aims to illustrate how the participants' experience of taking interferon-free therapies contrasted with their acknowledged

preconceptions of how that experience might be. These preconceived notions were rich with the predominant understanding of HCV treatment as a rigorous and demanding undertaking, informed by the interferon folklore that continued to permeate contemporary societal discourse. Whilst both physical and emotional side-effects were experienced during treatment, their magnitude and significance were diminished by comparison to the historical touchstone of interferon-based therapy, positioning them as relatively minor inconveniences and ailments which could be managed and overcome. Conversely, unforeseen difficulties such as a high pill burden for those on multi-tablet regimens contrasted unfavourably with assurances of improved treatment simplicity and straightforwardness.

7.3 Theme: An Honour and a Pleasure

7.3.1 A positive experience

The majority of participants related a positive and favourable account of their time on treatment, describing it as physically undemanding, a minor inconvenience, and nothing to complain about. The major exception to this discourse was Gary, whose narrative detailed a laborious and difficult treatment period, replete with a catalogue of side-effects reminiscent of a period of interferon-based therapy. This nonconforming case will be analysed in greater detail in due course. Primarily, however, the participants constructed their experience of interferon-free therapy as uncomplicated and relatively straightforward:

I'd, six o'clock at night, come home, have my dinner, take my inhaler, take my tablet, ten o'clock – bed. Nothing, nae, nae disruption whatsoever. Absolutely fantastic...

(Stewart, 52, single-tablet regimen)

I hate to use the term but it didn't, it didn't feel, I could say, if I was, y'know, at all arrogant or whatever 'oh it's a cakewalk, y'know, jus' go through the, the medication it's a cakewalk' I mean I could quite in a blasé way say that...

(John, 54, multi-tablet regimen)

Participants framed the short length of treatment as one of the most significant benefits of interferon-free therapies, with many reporting surprise and disbelief that

their treatment course had come to an end after such a relatively brief period of time. The reduced length of therapy was emphasized with the use of simile, described by one participant as “*like a sort a’ antibiotic treatment, it’s been that quick*”⁴¹, and for some, the benefits of a speedy therapy overrode any other apprehensions or concerns they may have harboured:

...that’s jus’ the way I look at it, y’know, I think positive like, y’know, I don’t think about the treatment going ‘oh it was terrible, it was this, it was that’, because it was quick.

(Steve, 45, multi-tablet regimen)

In addition to the comparatively rapid duration of therapy, the reduction in side-effects when compared to interferon-based treatments was also a significant element of the positive treatment experience, as previously described. For the majority, a comparison with interferon-based treatment was hypothetical, made through their socially informed understanding of what that therapy entailed. The two participants who had previous first-hand encounters with interferon-based treatment, however, were able to contrast their eventful and side-effect laden experiences with a relatively benign course of interferon-free therapy:

...it was all easy, compared to the last time, ‘cause I, ‘cause I done the treatment, the interferon one, an’ compared to that, this was a breeze [laughs], this was like, jus’ like taking y’know, Lemsip or something y’know...

(Keith, 54, single-tablet regimen)

it was really really – the only thing it was like, erm, mmm, I would say, even the side-effects, like being tired, it was like not the tiredness that I’d experienced with the other one...

(Happy, 51, single-tablet regimen)

Despite not yet knowing whether the treatment had been successful, a positive impact from the therapy was already apparent in a number of the narratives. Prudent optimism that the drugs had taken effect permeated the participants’ accounts, with

⁴¹ Keith, 54, single-tablet regimen

individuals cautiously expectant that they would obtain an SVR in due course. This confidence in the treatment was aided by beneficial physical effects noted by the participants during therapy, such as increased energy, and improvements to their complexion and general wellbeing. For Danielle, the positive aspects of treatment completion were not solely expressed in terms of health. She identified the end of her period of HCV therapy as a driver for more fundamental changes in her life:

...the last couple a' weeks of it, I was fine, absolutely brilliant, an' now, that it's finished, it's even better, my life's just totally changed altogether, I'm now working, everything has really changed for the best now, so, I'm glad I done it.

(Danielle, 43, single-tablet regimen)

Tellingly, there was scarce discourse around treatment failure, which, when mentioned, was generally positioned as a temporary state, and couched in positive language. Many participants recurrently remarked on the success rates of the drugs, with figures given of over 90% and in some cases 100%. Participants were sanguine, buoyant and optimistic about their futures even before their end of treatment blood tests had been taken and reported:

I'm no' going a' leave here today an' let it play on my mind I'm jus' going to, I'm jus' gonna come back in two weeks' time an' find out the, the results, .an' if it hasn't totally cleared, I'm feeling better, I'm looking, it's no' gonna beat me, y'know, I know what the situation is. I've totally changed aye, I've flipped fae one side to the other now like, I've even, even, partner says it, my sister says it, she says you're no' even bothered about it, I says nah, it's no', it's no' gonna get me down.

(Stewart, 52, single-tablet regimen)

Whilst previous accounts of interferon-based HCV treatment often construct it as an immersive and all-consuming experience (e.g. Hopwood and Treloar, 2005; Janke *et al*, 2008), the narratives generated within this study suggest participants were able to take a more disengaged and detached stance to an interferon-free therapy. Treatment was commonly framed as something which fitted into an existing life, and for which only minor adjustments and concessions were required. Because of this, participants were often able to take a step back from treatment, disconnecting themselves from the reality of their situation:

...an' it's been so successful, erm, I kind of do feel like – well, that was, it's like being in, almost, in a bad accident, but something that all happens round about you, but it doesn't actually affect you, somehow.

(John, 54, multi-tablet regimen)

7.3.2 Guilt

Whilst the participants' narratives surrounding their experience of interferon-free therapies were largely complimentary and positive, a perception that they had been fortunate and lucky to access these treatments underpinned the discourse. A number of individuals described feeling guilty at what they perceived as good fortune of being in the right place at the right time, underlining an understanding that interferon-free therapy was not commonplace and available to everyone, but a privilege and an honour.

I was really lucky, I got given my treatment within three years of diagnosis, I got put on the, the quicker treatment, the most effective treatment, I was put in all the right places, given all the right directions, an' then there's other people who were like... Maybe it's jus' me, jus' the way my mind works, but it did, I, I felt a, a bit guilty, an' a bit like, well, I've had more advantages an' a step forward than you.

(Gary, 38, multi-tablet regimen)

Feelings of luck and guilt were framed within the discourse as two sides of the same coin, and were compounded by participants favourably comparing their own situation to others with HCV, emphasising the differences in their own treatment trajectory to what were considered less fortunate individuals. These comparisons were made with people who were known to the participants, but also with the socially produced archetype of what HCV treatment *should* encompass. Despite any concurrent discussion of treatment side-effects, disappointments or hardships, the impression of feeling lucky to have gone through interferon-free therapy, and guilty of their experience in relation to others prevailed in all participants' narratives.

I'm glad I done it, I mean I'd tell anybody that was gonna start the treatment to do it, because I mean it's a lot better than what the other therapies have been, no' that I've been on them, but what I've heard about the triple therapy an' everything you dunnae go through anywhere near as much as that.

(Danielle, 43, single-tablet regimen)

Well, me personally, I've seen other people going through it, an' err, I'm very very lucky in comparison to what they looked like y'know...

(Steve, 45, multi-tablet regimen)

For John, the guilt he experienced was rooted in his perception that some degree of atonement should be necessary to cure a disease which he felt he had brought upon himself. The ease and simplicity of his treatment experience jarred with his belief that a penance should be paid for the removal of HCV from his life, and that he had got away lightly compared to others he knew. Throughout his discourse, John made a number of comparisons to close friends who lived with chronic illnesses, praising the way they coped with their situations, and denigrating his own struggle in comparison. John felt he had escaped HCV with impunity, and this unsettled him:

I'll tell you why I felt guilty about it – I've got a really close friend who's got like a, this medical situation, an' he copes with it brilliantly, an' he, erm, he hadn't, he hadn't caused it himself or anything, he was jus', y'know, erm, suffering from this condition, an' he marches through it brilliantly, y'know, and I've got another friend who's diabetic, an' I didn't even realise he was diabetic until fairly recently, and I've known him for a long time, an' I thought these people deal with these things all the time an' they have to struggle along an' get on with it, y'know, an' I've jus' been more or less given a solution to my problem an' have kind of got away with it scot-free.

(John, 54, multi-tablet regimen)

The term 'survivor guilt' has previously been applied in studies of chronic illness where patients compare themselves to others with the same diagnosis, but who may face a worse prognosis, such as in chronic myeloid leukaemia (Patenaude and Rapoport, 1982) or long-term non-progressors with HIV (Schönnesson and Ross, 1999). The concept of survivor guilt is now recognised as encompassing a broad and diverse pattern of health behaviour, and is commonly framed as an interpersonally driven emotion, aimed at mediating the relationship between the individual and wider society (Carni, Petrocchi, Del Miglio, Mancini and Couyoumdjian, 2013). Although no single widely accepted clinical or conceptual definition exists, a recent concept analysis by Hutson, Hall and Pack (2015) described seven attributes of survivor guilt which resonate with this study: the presence of loss; being spared from harm; that it is adversely experienced; individualised; interpersonal; variably manifested and context-

driven. Whilst discussion of survivor guilt within the context of HCV has remained absent from the scientific literature to date, journalistic accounts of individual experience (e.g. Olds, 2016) provide anecdotal support that the disparities in access to interferon-free treatments may be influential in creating a substantial cohort of individuals for whom a condition akin to survivor guilt may pose on-going concerns.

In addition to feeling fortunate in comparison to other people, participants' awareness of the cost of the drugs contributed to their sense of honour in receiving these therapies. Whilst feelings of shock and disgust at the expense of the medications were voiced, these views contributed to a sense of privilege in gaining access to medications which were not universally available. The price tags of these medications were not only discussed in relation to other treatments for individuals with HCV, but also in the wider context of distributive justice within other diseases:

Because I know they can't give it to everybody, because it is expensive, y'know, err, but, I got told, it'll be jus' like taking any drug after a long while – the prices go down. It's the same as anything, prices eventually go down an' that'll be, there won't be the injections any more it'll jus' be the tablets an' things, err, but I jus' felt so grateful that I could get it right now, while it's still that expensive.

(Steve, 45, multi-tablet regimen)

I: ...so you've had access to these drugs that are really expensive [K: thirteen thousand pound a month!]; how does that make you feel?

K: It makes me feel, bloody privileged, 'cause, y'know what I mean, 'cause no' many people are getting that, I mean there's people oot there that've got cancers an' stuff an' they're getting knocked back for treatments that cost that much.

(Keith, 54, single-tablet regimen)

A few participants mentioned the media as the source of their information on medication costs. However, a number of others implied that this knowledge was explicit in the discourse of the treating healthcare team, with participants trained in the price of their cure from an early stage:

I knew that fae, the first week, how much these, all these cost an' all that, I mean coming here you get taught, you get told what they're trying a' do here, an' you find out how expensive they all are...

(Stewart, 52, single-tablet regimen)

The inflated costs of the drugs, and the associated sense of privilege in accessing them, generated a discourse which positioned commitment to treatment as an important consideration. Participants alluded to the battles they believed had been fought by healthcare professionals on their behalf in order to secure access to interferon-free therapies. A perception imbued the narratives that those deserving of access to interferon-free medications therefore needed to be serious and dedicated to their course of therapy, presenting themselves as candidates worthy of treatment, or 'deserving citizens' (Rhodes *et al*, 2013):

...for [names specific DAA], it should be appreciated more, it shouldn't be taken just for a chancer, it should be for someone who's truly truly committed to taking it, an' also keeping healthy...

(Happy, 51, single-tablet regimen)

In addition to commitment *during* treatment, a perception emerged that the guilt and privilege felt at being able to access such expensive therapies had more enduring implications. The experience of being prescribed these drugs strengthened, or built a resolve in a number of participants that the investment made in them, both financially and personally, would reap long-term rewards.

I feel sort a' - so, it makes me, it'll make me think twice about going back taking drugs or alcohol or getting kind, going back on that kind a' thing when you, you've been privileged enough for people a' fight to get you better.

(Keith, 54, single-tablet regimen)

Similar findings have been reported previously by Rhodes *et al* (2013) in their study conducted during the interferon era. They interviewed individuals with histories of injecting drug use, and described access to treatment as constructed in terms of gratitude rather than entitlement. Hepatitis C treatment was an exception rather than an expectation among their participants, echoing the discourse of privilege and guilt

found in this study. Eligibility for treatment needed to be negotiated within a culture of limited treatment expectations even before the arrival of interferon-free DAAs presented additional restrictions and barriers. The notion of treatment ‘privilege’ is not solely a result of treatment rationing, but of historically produced rationed treatment expectations.

7.3.3 Theme summation

‘An honour and a pleasure’ unites the dialogue of a positive and encouraging treatment experience, with concurrent sentiments of good fortune and privilege. The reduced duration of treatment, perceived reduction in side effects and a prudent optimism in the efficacy of therapy combined to construct an optimistic and upbeat discourse, which positioned treatment as a routine component of life, rather than as a detached and all-consuming experience. Entwined within this perception, participants described feelings of luck and guilt at their own treatment trajectory compared to others in similar situations, and privilege at accessing medications known to be exorbitantly expensive. Interferon-free HCV treatment, although agreeable, was not portrayed as the norm.

7.4 Theme: Treatment needs

The theme ‘treatment needs’ grew from the combination of two unmistakable elements which pervaded the participants’ narratives: the discourse concerning support, and the approaches participants described in their search for treatment efficacy. These two components created a persuasive account of how participants continued to seek affirmation during a course of interferon-free treatment, and require professional involvement despite a perception that the drugs were easier to take.

7.4.1 Support: existing support networks

Participants described a range of existing support throughout their interviews which pre-existed HCV treatment, involving both individuals within their homes and wider networks of friends and professional support workers. John and Peter lived with long-term partners, Danielle lived with her mother and young child, and Happy and Gary lived with grown-up adult children. The remaining three participants reported living

alone, although as his narrative progressed it became clear that Stewart's long-term partner was a de facto resident in his house. In addition to family, many of the participants related details of friends whom they had confided in, as well as a number of support workers from various third sector agencies and charities working within the fields of drugs and alcohol, and blood-borne viruses.

Six of the participants therefore described comparatively developed and mature social support networks. However, the existing support networks of Keith and Steve were noticeably diminished in comparison to the others. For Steve, this was through personal choice. Following a period of drug rehabilitation, he had tenaciously avoided attending support groups or contacting anyone from his past, cutting himself off from a previous life. In addition, he described his family and friends as physically distant and unavailable, positioning himself as a loner:

...but, you got to remember, not a lot a' people like me, I mean likes I don't have any friends up here, or family up here, at all, y'know, mines are miles away, y'know, near a hundred mile away, so, err, I'm on my own...

(Steve, 45, lives alone)

For Keith, a lifetime of previous drug use also offered a potential reason for his relatively self-contained current life. He felt he had missed the opportunity to make long-lasting friendships and close ties due to the social circles he had spent much of his life moving in:

...you know it yoursel', the drug lifestyle can be a lonely lifestyle. Even though you've got acquaintances, that's all they are, they're acquaintances, they're no' friends. You maybe take drugs wi' them but then you go away, an' live in your own wee world.

(Keith, 54, lives alone)

Existing support networks therefore varied between the participants. However, their narratives were consistent in the primacy given to the support provided by healthcare professionals during their treatment regimens, as will now be examined.

7.4.2 Healthcare professionals

Participants eulogised the support and care provided by the healthcare professionals who were directly involved in prescribing their HCV treatment. Accounts of their encouragement, professionalism and patience were commonplace within the narratives, with participants often extolling the sense of connection they perceived with their nurses and doctors. At times, the descriptors used by participants to illustrate the therapeutic relationship evoked a deeper sense of belonging:

...you guys give me the support, even the hug (...) that my family couldn't give me because they're far away, an' I say, an' for me, I feel like you people are my family looking after me, it's actually better, because my family can look after me but they don't have the tablets!

(Peter, 51, single-tablet regimen)

The care provided was not solely focused on the practicalities of HCV treatment, but viewed as a broader and more comprehensive type of support, encompassing the emotional care of the participants and their multi-morbidities. Support was framed as something holistic, focused on the complete individual rather than on the treatment of a disease, and the time taken by health professionals to listen to participants' wider concerns was particularly prized:

...aye, you're supporting people, you're giving people a purpose, if you get what I mean. No' just for a' get your treatment, but ken others things, to come up for a cup a' coffee an' a chat (...) or talk to the nurses, or talk to the lassies at the front desk an' stuff...

(Keith, 54, single-tablet regimen)

...jus' being able a' pick up the phone, an' jus' – have a, even, an' jus' have a laugh an' say "ah, shut up Gary, you're being silly" or – it can be as simple as that (...), helped me massively. Like, like, I owe them my life as far as I'm concerned, quite literally, that's how I feel, that's how much of an impression people have made here, for me...

(Gary, 38, multi-tablet regimen)

The discourse from those with a significant history of drug use intimated the support experienced differed from some of their previous encounters with healthcare. Discrimination towards substance users by healthcare professionals has been widely reported for many years (van Boekel, Brouwers, Van Weeghel and Garretsen, 2013),

with negative attitudes from health professionals associated with a detrimental impact on treatment outcomes and patient self-esteem. In contrast, some participants in this study spoke of being treated exceptionally, like “*some kind of VIP*”⁴². However, the overriding sense was of normality; an appreciation of receiving a level of care commonly experienced by the wider population:

...this hospital's a delight, an' everybody I've spoken to agrees with me, they say it's amazing, how you get treated, jus', jus' absolutely normal, like anybody else an', that's exactly what I've felt...

(Steve, 45, multi-tablet regimen)

This positive perception of the support provided by healthcare professionals to participants during their treatment featured extensively within the narratives. For the four participants who engaged with a local respite facility run by a third sector HIV and HCV charity, this positive perception also extended to their time spent there. Support from professional quarters emerged as more integral to the experience of HCV treatment than support provided by family and friends, and whilst incidences of support from other sources in their established networks *were* mentioned, they largely appeared as isolated anecdotes, delivered to order when prompted by the interviewer. A couple of participants disclosed how concern from family members could often become more tiring than helpful, and almost necessitated a reversal of role resulting in the participant supporting *them*:

I mean like, [my son] would be phoning up, and asking my wife “how's dad, what is he, y'know, is he, doing all these...” y'know, they were suggesting all these mad side effects I might be having, erm, and even [my daughter] y'know, who's phoning up an' saying, erm, y'know, she's imagining that I'll be, y'know, having difficulty with the medication, an' I was having to convince her “Look, I'm fine” y'know...

(John, 54, multi-tablet regimen)

I think [my partner] been too many hours on the internet. Too many. Him, and my brother, because they were calling each other, an' when they hear that, one said to the other, well you check if he has this, you check if he has that, an' I say, guys! It's too much!

(Peter, 51, single-tablet regimen)

⁴² Gary, 38, multi-tablet regimen

One notable exception to the positive discourse around health professional support during therapy came from Danielle. For her, a feeling that she had not received the support she should get during treatment was evident, with her narrative recounting feeling abandoned and neglected by healthcare professionals, and being left with an onus to monitor her own welfare. As discussion progressed, an understanding emerged that these feelings were positioned in relation to people who had received other, interferon-based HCV treatments, and a perception grew that she felt short-changed by her interferon-free experience:

I jus' felt you didn't have enough sort a' communication wi' people, erm, like [the HCV nurse] maybe phones me, oot the whole treatment, I think she contacted me three times, oot the whole treatment. An' I think, d'you know, it was like you were jus' left to get on wi' it, erm, if you need any help jus' phone us, but I'm that sort a' person I'll no' ask for it, y'know what I mean? So I do think that's what they really need to gi' people a bit more support through it.

(Danielle, 43, single-tablet regimen)

...oh, I don't know how a' explain this one really. I think people are all getting treated differently, right, when you're on triple therapy, right, you're getting all the support, all the support, money-wise, mentally, the doctors, all the rest a' it, this therapy you dunnae get nothing.

(Danielle, 43, single-tablet regimen)

Support was a treasured commodity for Danielle, and the perceived absence of any value-added services and care during HCV treatment had a significant detrimental impact on her experience, leaving her feeling cheated that she had had to rely on her existing support network alone. When explored further, it became evident that Danielle's narrative on the value of support during treatment shared key insights with other participants.

7.4.3 Perspectives on the value of support

A sharp contrast became evident in the perceived value of support during a period of interferon-free HCV therapy between participants who recounted an extensive and graphic history of drug use, and those who did not. Stewart, Happy and Peter related uncertainty as to where their infection had originated, and their discourse positioned

themselves apart from drug using communities. John, who had contracted HCV through drug use in the 1980s, also fell into this group as he constructed an account of his life which placed his drug-using days in the dim and distant past. For these individuals, support during treatment, although gratefully received and highly regarded, was ultimately deemed unnecessary on retrospective reflection:

In retrospect, now that you ask me that, I can quite clearly say, erm, y'know, I could have breezed through that without telling anybody, and, if I really chose to, I wouldn't have needed any support through the actual medication itself. If I'd realised it was going to be that easy, I wouldn't have been freaking out about it beforehand.

(John, 54, multi-tablet regimen)

I: Because you were feeling good though, did you need that support?

S: Err, no' really, I was, I was really helping myself, mostly helping myself, I don't think I'd, honestly, two, two tablets down, an' I dun even think about it, jus', it jus' went out my head...

(Stewart, 52, single-tablet regimen)

No, no, not at all, no, no. No. Not with [names medication], nothing at all, I never felt I needed any support with [names medication], not at all, not at all.

(Happy, 51, single-tablet regimen)

By contrast, Keith, Steve, Danielle and Gary all related contracting HCV through injecting drug use, and their narratives were rich with stories of addiction, drug taking and attempted recovery. Their discourse emphasised the significance of support, highlighting its value to both the practical and emotional aspects of treatment:

...it is quite hard to jus' keep it, doing it yourself, unless you've got somebody to remind you, err likes, like I said, to wake you up in time an' things like that, it's really quite difficult, erm, you may think oh it's easy jus' take it err next, nine in the morning, nine at night, but likes, when you're not working an' you're likes, err, like I said, really heavily medicated, it doesn't work out like that...

(Steve, 45, multi-tablet regimen)

I: Was support important to you?

K: Aye, it was good to come here.

I: Why?

K: *The mental, the friendship, the feeling a' care, people caring about you, d'you get what I mean? If you do that in the community you're jus' going in a' see somebody, you're getting your tablets an' you're fucking off for three months, it's no' gonna be the same. You're no' gonna have that...*

(Keith, 54, single-tablet regimen)

The importance of support is ingrained into the substance use recovery agenda, with many studies highlighting the importance of structural and functional components of support to an individual's recovery trajectory (e.g. Day *et al*, 2013). Adaptive changes in social networks from those supportive of illicit substance use to ones that are supportive of recovery have been shown to have a positive impact on sustained abstinence (Boisvert, Martin, Grosek and Clarie, 2008), and are often mediated by referrals to mutual-help groups such as Narcotics Anonymous (Kelly, Stout, Greene and Slaymaker, 2014). Social support is a prominent and fundamental cornerstone of the substance use recovery discourse, and for those participants who had engaged with drug treatment in the past, the collected narratives suggest that this understanding of the importance of support had filtered through to other aspects of their lives. For these participants, support was not framed as an additional bonus to HCV therapy, but as an expected and essential component of the HCV treatment package. A culture of support has been built around individuals who have engaged with drug recovery, which, when bolstered by the legacy of interferon, has been applied to expectations of HCV therapy:

Even with the new treatment, I think you need that support there, no matter where it may come from. Jus' someone saying here, there you go, like you would at your pharmacy an' no' having any, I think that puts people onto an illusion of fear, an' it prob'ly confuse more people, an' an', an' on balance, I think, from my own point of view, that err, I would be quite sceptical about jus' turning up in pharmacy having my drugs an' then not having an angle, or no' knowing that there's someone to talk to after it, an' no putting as much in...

(Gary, 38, multi-tablet regimen)

For these individuals, support has become an expected commodity, where increased contact with professionals, added services, and greater provision of resources when delivering an intervention are de rigueur. Experience of HCV treatment is shaped by

an expectation that added support will be available, and a high degree of importance is placed on obtaining and utilising it rather than relying on existing networks. A need for support grows out of these expectations, despite an acceptance and awareness that the treatment has improved:

An' you also need somebody that's a professional like, especially in the hospital so you can talk about the treatment, 'cause most people'll not talk to their partners, or their friends or their family about the treatment, 'cause they don't know about it, an' it can, it can really freak them out I suppose, so you do need a professional to speak to, 'cause you will have low days an' different days, but likes a', it's, it's a great treatment.

(Steve, 45, multi-tablet regimen)

Support was not the only need which emerged from the participants' discourse, as a need to know that the treatment was working also became apparent. This search for efficacy during therapy manifested itself in a number of forms which will now be examined.

7.4.4 Searching for efficacy: hunting for side-effects

The lack of physical effects from the medications led to doubts around the efficacy of the drugs. Participants expressed concerns that the scarcity of side-effects equated with a reduced effectiveness, querying the authenticity of the medications they had been given. A discord arose between the interferon-influenced expectations of how a course of HCV treatment should be, and the general lack of physical side-effects that were subsequently experienced:

Nothing happened at all, an' I'm like, have they, have they gave me dummies? What's happening here? I should be ill. But nothing, absolutely nothing happened...

(Stewart, 52, single-tablet regimen)

...when I came after four week I ask [the HCV nurse], I say, she said do you feel anything? Are you tired or this? An' I say no, I say actually sometime I think I'm on a placebo, because there is no any effect at all.

(Peter, 51, single-tablet regimen)

D: *...it jus' made me think, 'cause I was expecting something totally different, I think I was expecting to feel, if it was working there was going a' be a sort a', an effect to me, that would notice that it was working...*

I: *Like a physical...?*

D: *Aye, an' there was none a' that, I was thinking well, should I no' be being sick an' all the rest a' it, all the time?*

(Danielle, 43, single-tablet regimen)

The belief that HCV treatment should be a rigorous and onerous undertaking, rather than a straightforward and undemanding process, constructed a compelling discourse relating how participants subsequently searched for signs and indicators that their treatment was working. A need to substantiate the effect of the drugs permeated the participants' narratives, shaping a perception that side-effects were almost desirable and advantageous:

J: *I mean, you wrack your brains looking for possible signs of side-effects, an' you kind of start to imagine them a little, y'know? Err, little things get exaggerated in your head, y'know – I'm feeling a bit tireder than I normally do, or would I? No? No, no after all, y'know, you were busy doing this, and doing that, you've been running about – you're just tired like anybody else, y'know?*

I: *Why do you think you're wracking your brains?*

J: *I don't know, it's jus' looking for signs really...*

(John, 54, multi-tablet regimen)

This hunt for side-effects increased the likelihood that any physical irregularities experienced may be attributed to treatment, despite an awareness that transient ailments can occur at any time, whether taking HCV therapy or not. This perception was not confined to the participants alone, but conveyed in accounts of how friends and family were also eager to attribute non-specific symptoms to the drugs:

...when I took the tablet at lunchtime, twice, with a meal, after couple of hours I have diarrhoea. But, I thought, I cannot, know everything that happen I cannot relate it to the tablet, because without treatment, sometime happen that you eat something an' then you have diarrhoea. So, because every time I

say something, [my partner] say you no' telling me! An' I say, because, if I say to you, oh, I jus' have diarrhoea, you would relate it to the treatment an' maybe it was your cooking!

(Peter, 51, single-tablet regimen)

Side-effects attributed to medications are typically viewed unfavourably, and have been frequently linked to poor medication adherence in HCV treatment (e.g. Sublette *et al*, 2015). A small body of literature from other disciplines indicates patients may sometimes interpret such symptoms as indicating drug effectiveness. For instance, studies concerning patient perceptions of rheumatoid arthritis medication have described side-effects as a natural reaction to 'powerful' drugs (Lorish, Richards and Brown, 1990; Goodacre and Goodacre, 2004), and research in the field of oncology continues to describe patients equating toxic therapies with increased efficacy as previously discussed (Gradishar, 2015). The insights gained from this study feed into this discourse and provide a new perspective on the experience of side effects during a period of HCV treatment. Participants actively sought out adverse effects from interferon-free treatments as biomarkers for the effectiveness of the drugs.

7.4.5 The importance of results

The identification of possible side-effects was not the only method by which markers of efficacy were sought however. The importance to participants of hearing how they were progressing through treatment from healthcare professionals also became a recurring refrain within the narratives. Routine blood tests to monitor the HCV viral load were taken two to four weeks into treatment, and the significance of receiving these blood test results detailing the downward trajectory of the HCV viral load was emphasised repeatedly, and provided reassurance that the drugs were taking effect:

...it's went down fairly rapid, y'know what I mean, within the three months, ken what I mean, even though I've only been taking it for three months it's jus' went wham [indicates a downward trajectory with his arm], an' hearing results has been like, good, sort a' like, oh it's working, 'cause it gives you that, that thing, that it is working ken if it's going doon an' doon an' doon...

(Keith, 54, single-tablet regimen)

...I started off really high, I was [x] million, which is very very high, an' I went down to [states much lower figure] within three weeks – that's impossible. I never thought that was even possible. Err, so, it's when you find out how quickly the treatment is working, err, in the first three-week period an' you're thinking – that's only three weeks, so it gives you that massive hope, y'know...

(Steve, 45, multi-tablet regimen)

In addition to providing reassurance about the drug's efficacy, and strengthening hope for a successful treatment outcome, the viral load results were also motivators for participants to continue adhering to their HCV treatment regimen, in the face of scant physical evidence that they were making any progress:

I had to like, phone them, an' erm, they were – [states result of most recent viral load test], I was, I mean I couldn't even believe it, there was, I was asking, I say, oh – write it down, let me see! [States starting viral load in disbelief] - y'know, that's, like motivation to, kind of really made me like be more determined, I, I have to clear this...

(Happy, 51, single-tablet regimen)

The value of laboratory medicine is most often spoken about in terms of supporting clinical decision making, patient safety, health economics and resource management (Hallworth *et al*, 2015), but rarely in terms of the patient experience. However, these insights stress the value that participants taking interferon-free HCV therapies placed on hearing encouraging test results, situating them as beacons of reassurance, hope and motivation and implicitly demonstrating a surprising degree of health literacy when compared to other conditions. For example, Wolf *et al* (2004; 2005) described poor understandings of HIV viral load and CD4 count amongst American cohorts of HIV positive individuals receiving anti-retroviral therapy in the late 1990s and early 2000s, correlating limited literacy skills with a poor appreciation of biomedical results. More recent work continues to describe this association in HIV (Laws, Danielewicz, Rana, Kogelman and Wilson, 2015), suggesting the literacy of participants within this study may have played a role in the value and significance they ascribed to laboratory test results. Unfortunately, educational achievement was not recorded within the collected demographics and is a limitation of this study. However, it would provide a fertile area for further investigation.

The dialogue concerning the importance of results also resonates with the growing scientific discourse around 'self-tracking' and the 'quantified self'. Although these terms have emerged in response to the increasing use of wearable technologies in the monitoring of personal health, and the focus of self-tracking is more commonly framed around the concept of healthism than degrees of illness, the primary objective of self-tracking is the achievement of self-knowledge through numbers (Lupton, 2013). The quantified self uses technology to invest individuals in health decisions, moving them from passive recipients of healthcare to active participants in their treatment, by framing the numeric data generated as direct access to a truth about the self (Abend and Fuchs, 2016). As Lupton (2013) argues, as bodily states and functions become ever more recordable and visualised, it becomes easier to trust numbers over physical sensations.

7.4.6 *Feeling better*

That is not to say that physical sensations did not play a role within the treatment experience. In addition to seeking out side-effects and focusing on laboratory tests, a couple of participants described a further instinctive approach to evaluating the effectiveness of treatment: they simply felt better whilst taking it. Primarily describing a feeling of reduced fatigue, these accounts begin to provide context to quantitative measures of HRQoL which have reported improved scores from interferon- and ribavirin-free HCV regimens during the period of therapy (Younossi *et al*, 2015):

...maybe the hepatitis made me slow down but I didn't realise, an' I thought it was jus' age! An' then I thought, I supposed to be feeling less energetic [on treatment], but, I want to do things all the time (...), it was fantastic, because I, I was feeling better after the four weeks, I say I feel more energy, where before by the end of the day I feel like I did too much, an' with this is was not.

(Peter, 51, single-tablet regimen)

Aye, it, it got even better, I mean, you'll no' see it now like [rubs belly] but, I mean all my fruit smoothies, my shakes, I've got a belly now [chuckles] after the eating, erm, there's no', I haven'ae, there's no' one day where I've went back, err, jus' lay about, I'm, I'm up, I have to, go clean something, or do something, or go a' work, I'm no' at the jogging stage yet like [smiles] but, it's jus' euphoria jus' took over since I've been on [the tablets]...

(Stewart, 52, single-tablet regimen)

Whilst anecdotal, it is interesting to note that the HRQoL domains in which on-treatment improvements met the minimal clinically important difference in the study by Younossi *et al* (2015) were vitality and general health, two concepts which undeniably resonate in the quotations above.

7.4.7 Theme summation

The 'treatment needs' theme comprises two main elements: the prevalent discourse around support which featured heavily in every participant interview, and the need to know the treatment was having an effect. In general, participants were overwhelmingly positive about the support they received through treatment. However, retrospective reflections on whether this support was necessary varied in line with their past experiences of drug use and recovery. For those participants who had a significant history of drug use, additional support from healthcare professionals and third sector agencies was constructed as a greatly valued and integral part of HCV treatment, despite an awareness that the actual therapy was much less physically demanding than interferon-based regimens. In addition, the dearth of physical side-effects from the drugs led to participants seeking reassurance that they were taking effect through a combination of approaches, the search for side-effects, the importance placed on blood results, and the self-assessment of improvements in their own wellbeing. These strategies were employed in lieu of more obvious manifestations of drug action, and provided encouragement, reassurance and motivation to continue with therapy.

7.5 A nonconforming case

7.5.1 The case of Gary

The strength and credibility of an analysis can be tested by how well it relates to exceptions to the rule. So-called deviant case analyses can illuminate and enhance the thematic patterns within the data, producing a richer, more in-depth understanding of the phenomenon in question (Silverman, 2013). Gary's experience of interferon-free HCV treatment grated with the predominant discourse emerging from the other participants, contradicting the largely positive and optimistic outlook espoused by the majority. His narrative was rich in the detail of an eventful and arduous treatment period, and began with an extended account of the many side-effects he had suffered

in the early stages of treatment. The experience he related was reminiscent of a period of interferon-based therapy, recalling both the physical and psychological side-effects commonly experienced with that drug:

...but anyway we got to the third week, erm, I started getting quite violently ill, sick, migraines, constant headaches were coming along, I spent about two weeks, literally, feeling like vomiting, couldn't move off the sofa, lying in the same clothes, never had any energy, very lackadaisical, very very aggravated, I got myself so agitated, they ended up putting me on erm, chloropazine [sic], 'cause a' my, I was so, getting so stressed...

(Gary, 38, multi-tablet regimen)

Whilst Gary was not alone in experiencing side-effects, his account was unusual in the prominence he gave them. He characterised his experience of treatment as one of illness and disorder, in contrast to other participants whose narratives mainly emphasised wellness and vitality punctuated by occasional complaints. Gary constructed a self-fulfilling prophecy, embracing the negative experience of HCV treatment that he had predicted and prepared for:

... 'cause I jus' said that to my daughter it must been about two-three days ago, I said it's bizarre, I said like, here I am, as I am, all, getting on wi' it, an' in three days time I start medication, erm, I could, look like I'm, I'm on death's door...

(Gary, 38, pre-treatment interview)

...an' then it got to six-seven weeks, jus' before I went into [the respite centre] that's when I kinda had that, I didn't feel ill before [I started the treatment], an' now I feel like, at death's door.

(Gary, 38, post-treatment interview)

An association between the expectation of treatment side effects and the subsequent realisation of those symptoms has been repeatedly shown in other conditions. For example, Mondaini *et al* (2007) demonstrated that sexual side-effects from a β blocker drug were reported three times more frequently amongst a group of patients specifically informed about that potential side effect, in comparison to a control group who were not. Similarly, Nestoriuc, Orav, Liang, Horne and Barsky (2010) described an association between heightened concerns amongst patients prior to starting arthritis medications, and a subsequent higher incidence of side-effects during treatment.

Whilst this phenomenon is widely reported, the expectation of a difficult and demanding course of interferon-free HCV therapy was widely held amongst the participants and not limited to Gary. Therefore, why was he alone in having his worst expectations confirmed?

Whilst it is possible that these medications may have severe adverse side-effects for a minority of people taking them, the nocebo phenomenon, in which placebos produce adverse side-effects, has also been used to offer insight into the reporting of nonspecific side-effects in patients taking active medications (Faasse and Petrie, 2013). Patient expectations and pre-treatment conditioning are often designated as key components of this phenomenon, and Gary's narrative displayed a depth and intensity of expectation which was noticeable among the collected testimonies, positioning temporary illness as an absolute necessity in order for his therapy to be effective:

...I, I, I kinda got to that stage where I knew, for treatment to be successful, there's gonna be, there's gonna be elements a' illness in there, it's gonna do things to your body, so – aye, I kinda jus' kept my mind in that...

(Gary, 38, multi-tablet regimen)

...jus' because I knew, listen, this is part of it, an' I kinda structured my mind so I know I've gotta get ill to get better type a' thing.

(Gary, 38, multi-tablet regimen)

In addition to expectations and patient conditioning, a range of further factors have been associated with the nocebo effect, including psychological characteristics of the individual, physical and symbolic features of the medication itself, and situational and contextual factors (Barsky, Saintfort, Rogers and Borus, 2002). Gary lived with his grown-up children who were no longer dependents, and he had limited work commitments due to the voluntary nature of his occupation. The comparatively commitment-free setting of his narrative provided Gary with the freedom to realise his worst HCV treatment expectations, and granted him permission to act in ways which would otherwise be socially unacceptable. In addition, the HCV treatment also

provided Gary with a plausible explanation for other comorbidities which he possibly found less easy to address:

I suffer from anxiety and depression at the best a' times, so aye, it was easy to point to the treatment an' say "aw, I'm feeling like this because it's the treatment" even though, I know, if I wasn't taking treatment, I'd be having days like that anyway, so aye, I suppose it makes it easier on your whole mind and body jus' to say well, that's the treatment, an' then it kinda takes you off-a that it's not jus' my head...

(Gary, 38, multi-tablet regimen)

In contrast, other participants' accounts principally emphasised the importance of maintaining normality and routine during their therapy, and not wishing their pre-treatment concerns to be realised. John had not disclosed his HCV status to his employers and therefore wished to continue working full-time during his treatment period. Danielle repeatedly expressed concerns over how she would be perceived as a mother if she allowed her routine to slip. For Happy and Keith, a desire not to repeat their previous interferon-based treatment experience was manifest, and as Peter was self-employed, any significant adoption of a sick role may have considerable financial implications. Whilst Gary expressed hopes that his treatment would not be as laborious as he imagined, there was a distinct lack of such mitigating circumstances in his narrative. Indeed, Gary's account reveals a set of circumstances which combined to form a perfect storm. His unambiguous pre-treatment expectations of an arduous and intensely disruptive HCV therapy, conditioned by his understanding of interferon-based treatment, were supported by a comparatively commitment- and dependent-free personal situation which allowed these expectations to be fully realised and assumed.

At first glance, Gary's narrative seems contradictory to the prevailing understandings of interferon-free HCV treatment which have emerged from the thematic analysis of this data. Discussion of interferon-free treatment as a mild inconvenience or relatively benign is inconsistent with the central thrust of Gary's account. However, rather than disproving the analysis, this deviant case reinforces some of the key findings previously discussed, and emphasises the importance of considering the themes collectively,

rather than in isolation. Although at odds with the idea of interferon-free treatment as a generally positive experience, Gary's narrative strengthens other themes within the data, such as the discourse previously considered around treatment needs and the hunt for efficacy. The side-effects he experienced were borne of a belief that HCV therapy needed to be powerful and potent, and the more toxicity he experienced, the greater the chance of the treatment working. His testimony suggests that despite his difficulties, he believed the treatment he was taking was having a curative effect:

I never ever thought to myself I'm gonna stop this treatment, but there was, that niggling in the back of my head saying – can you carry on? I thought, no, I've come this far, I'm, I'm not gonna back out an' stop my treatment, no matter how hard-core it is...

(Gary, 38, multi-tablet regimen)

Gary's narrative also reinforces the importance of HCV treatment-specific support to individuals with significant drug histories. Whilst he positioned his family and close friends as a valuable support network, his testimony also recounts how access to wider groups of professional support workers and peers with the same diagnosis was particularly prized. By becoming ill during his treatment, Gary maximised the supportive value of his therapy:

Erm, there's mainly really jus' me an' my daughter, erm an' a few close friends that, that was my support up until I started networking wi', wi' everybody down at [the respite centre], an' then obviously that opened up so many more avenues, erm, so many more support workers an' people to talk to...

(Gary, 38, multi-tablet regimen)

Whilst initially appearing divergent from the prevailing discourse surrounding interferon-free HCV treatment, a closer examination of Gary's narrative reveals how it strengthens and augments many of the key themes found within the collected data. Although he did not experience the primarily positive experience of treatment constructed by the other participants, he did acknowledge the luck he felt at receiving it, and assembled an account which reinforced the discourse concerning treatment needs. In addition, Gary's narrative accentuates the importance of a contextual understanding of interferon-free treatment. He realised and embraced his interferon-

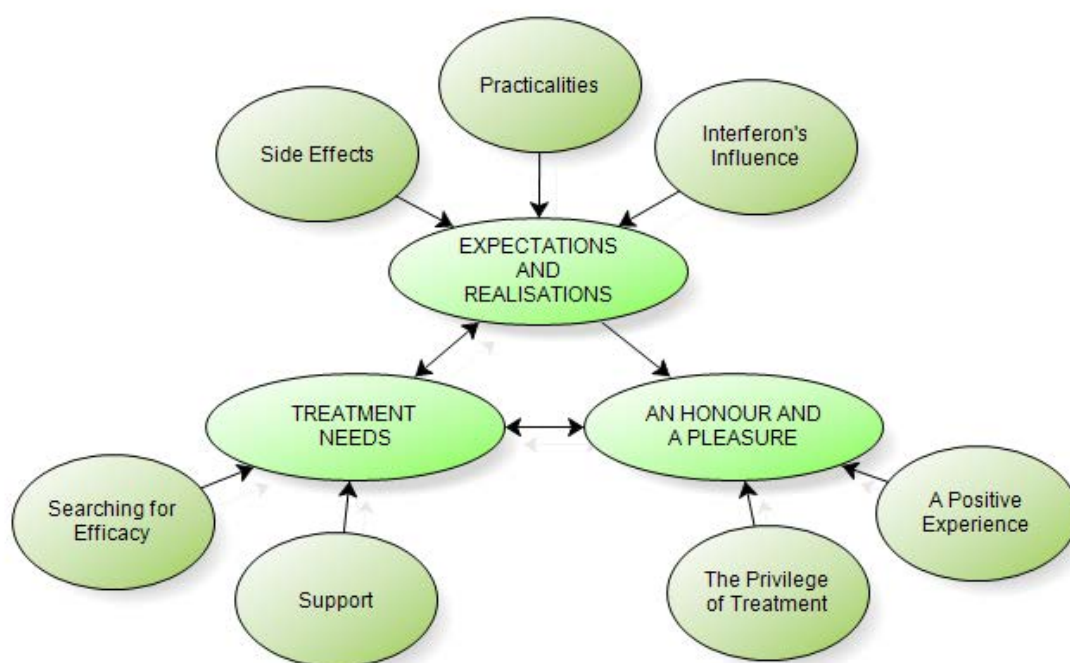
based pre-treatment expectations due to his understanding that HCV treatment *should* be gruelling in order to work, but also because his social and personal circumstances allowed him to.

7.6 Discussion

7.6.1 The relationship of themes

The intersubjective experience of interferon-free HCV treatment constructed by the participants is well illustrated by the three overriding themes previously described. These themes do not exist in isolation, but interweave, connect and collide within and between each individual narrative, demonstrating how understandings which have been presented here discretely are necessarily intertwined. Reflecting on the interplay between these themes and their relationship to each other, produces a more complete understanding of the lived experience of interferon-free HCV treatment, which is much richer than the sum of its parts (figure 1).

Figure 1: A pictorial representation of the themes and sub-themes which encapsulate the lived experience of interferon-free HCV treatment described and illustrated within this analysis.



The theme 'expectations and realisations' has intentionally been presented first within this analysis, as it acts both as a precursor to the treatment experience and also as a foundation upon which the subsequent themes are built. The influence of interferon-

fuelled expectations of treatment lies at the heart of the other theme constructions. For example, the positive experience and feelings of privilege espoused in 'an honour and a pleasure' are not produced in a void, but in relation to the growing awareness that treatment was not corresponding to preconceived expectations. Similarly, the hunt for side-effects and importance of support illustrated within 'treatment needs' are hinged on understandings of how an interferon-based period of treatment *should* be. The pervasive authority that the drug interferon continues to exert over expectations of interferon-free regimens is central to how these newer therapies are then experienced and realised. Interferon-free treatment is positioned in relation to understandings and perceptions of interferon-based therapy, it does not stand solely on its own merits but in comparison to what might have been.

The two other themes may at first appear the antithesis of each other. Consider the apparent disjoint between the theme 'treatment needs' and the relative ease of therapy proposed by 'an honour and a pleasure'. If treatment was relatively benign, then why were individual needs positioned so centrally within the narratives? Rather than being oxymoronic, such tensions highlight the manner in which each theme is fundamentally contingent on the other, and how examination of themes in isolation may lead to a limited understanding of the overall treatment experience. For example, a treatment experience which failed to correspond with pre-treatment fears fed the notion of 'an honour and a pleasure', focusing participants on the positive aspects of their therapy and creating an understanding that they were lucky to evade a more gruelling treatment trajectory. In doing so, concerns and doubts about the treatment emerged. How could such a relatively benign therapy be working, and what implications did that have for the provision of support? 'Treatment needs' grew from the insights and understandings gained from 'an honour and a pleasure', rather than in opposition to them.

Although the above example traces a linear movement, the interaction between the themes of 'treatment needs' and 'an honour and a pleasure' was reciprocal and dynamic in nature. For example, the self-monitoring and importance of support described within 'treatment needs' was not only the product of participants questioning an easier than expected time on treatment, but was also integral to the

construction of that positive experience. Hearing encouraging blood results, noticing improvements in general health and wellbeing, and feeling supported and cared for were part of the foundations upon which 'an honour and a pleasure' was established. These themes reinforce and enhance one another, emphasising the interrelation and unity of the analysis.

This is not to say that conflict does not exist. For example, the accounts of both physical and emotional side-effects discussed in 'expectations and realisations' sit uneasily next to the discourse which described participants hunting for non-existent side-effects in 'treatment needs'. How can both these positions be part of the same experience? These two positions should be considered in counterpoise to one another, where equilibrium was maintained between the volume and intensity of side-effects experienced and the proactive search for further signs of efficacy. Where few side-effects were noticed, a greater emphasis was placed on hunting for them, and where the treatment experience was defined by side-effects, the search for efficacy was deemed unnecessary. Consider the conflicting testimonies of John and Gary. John's account of searching for side-effects and evidence that the drugs were working is situated within a narrative which barely mentions any detrimental effects from the treatment at all, whereas Gary, who experienced a treatment period laden with side-effects, instinctively felt that it was taking affect:

I mean, you wrack your brains looking for possible signs of side-effects, an' you kind of start to imagine them a little, y'know? Err, little things get exaggerated in your head, y'know...

(John, 54, multi-tablet regimen)

...even though it does have its negatives, it, it's been nothing but a positive in the long run. An' I know it's knocked the shit out a' me, but at the same time I know, that doing that it's having an effect – to kill off the hepatitis.

(Gary, 38, multi-tablet regimen)

Although these accounts represent extremes of the scale, they illustrate the way in which apparently contradictory aspects of these themes wax and wane in relation to each other, emphasising the fundamental way in which the themes described are interdependent.

The nonconforming case study of Gary also highlights an important consideration. These themes must be considered within the context of the individual. There are numerous personal, psychological, situational and contextual factors which have been identified as potential components of the placebo phenomenon (Barsky *et al*, 2002), and whilst the thrust of this analysis stems from a realisation of largely unmet pre-treatment expectations, there may be particular individuals whose specific set of circumstances and attributes allows those expectations to be realised. This analytical model therefore provides a platform on which to base understandings of patient treatment experience with interferon-free HCV regimens, but does not claim to be applicable to each and every individual prescribed these therapies throughout the world.

Chapter 8

Discussion

8.1 Introduction

8.1.1 A brief overview

This thesis began by illustrating how the growing authority of HCV as a public health priority provided impetus for the rapid developments in drug therapy which have been observed over the last five years. The arrival of interferon-free regimens in clinical practice has improved the success rate of HCV treatment to over 90%, whilst substantially reducing the burden of side-effects and radically shortening the length of therapy compared to previous interferon-based standards of care (Asselah *et al*, 2016; Pawlotsky *et al*, 2015a). This sea-change in the nature of HCV treatment has been hailed as the dawn of a new era in the fight against the disease (Chung and Baumert, 2014), and has bolstered academic discussion of conceivable global eradication (Borgia, Maraolo, Buonomo, Scotto and Gentile, 2016; Hagan and Schinazi, 2013). It also constitutes the underlying rationale for this study's re-examination of the lived experience of HCV and its treatment.

A qualitative focus on individuals living with HCV has long provided insight into how the disease and its treatment are understood and experienced (Miller *et al* 2012; Treloar and Rhodes, 2009). This paradigm offers rich and nuanced understandings of the personal burden of illness, giving a recognisable voice to the decrements in HRQoL which are commonly reported in the quantitative literature (Speigel *et al*, 2005). However, the wealth of qualitative research in this area was conducted during the interferon era, and it is reasonable to speculate that the significant advances in HCV treatment observed in Scotland over the last five years may have influenced how the disease is being perceived and realised by those it affects. Experience is, after all, mediated by its social context. The timely re-examination of the lived experience of HCV and its treatment within this thesis is therefore justified, and the research questions which have guided this endeavour were founded on this reasoning. An empirical study involving qualitative interviews with 20 individuals living with HCV was undertaken. Eight of these individuals were followed longitudinally and re-

interviewed after a period of interferon-free HCV treatment. The generated data were interrogated using a thematic analysis, and the preceding four chapters have aimed to explore the major themes which were evident within the participants' narratives. These chapters have drawn on relevant social theories, and other published works to help illuminate the findings. In doing so, each chapter provides a detailed analysis and interpretation of one facet of the inter-subjective experience of living with HCV, or in the case of chapter seven, a multi-themed exploration of interferon-free HCV treatment.

8.1.2 Chapter aim

In order for a more integrated and meaningful understanding of the participants' lived experience to be achieved, the aim of this chapter is to contemplate the broader 'collective' stories told by the participants. How do these themes articulate with the wider discourse of HCV and its evolving treatment? The original research questions will be addressed by reflecting on the themes collectively, and examining the factors which underpinned the participants' experience. Why the themes exist as they do, and what conditions gave rise to them will be interrogated. Following this, the limitations of the study will be considered, prior to discussion of the implications this work may have for policy, the organisation and delivery of treatment, and individual clinical practice. The chapter ends with a personal reflection on conducting the study and a clear statement of the contribution to knowledge made.

8.2 Addressing the research questions

It is prudent, in this final chapter, to return to the original research questions which guided the empirical work conducted within this thesis (section 2.4.4). These questions form the fundamental core of the study, and relating the analytical findings to the central research problems identified must be the ultimate objective of this endeavour. The following discussion has therefore been structured around addressing each of the three research questions explicitly, and considering what the analytical themes mean in relation to them.

8.2.1 Question one

How is living with hepatitis C experienced and understood within the context of a new era of treatment?

8.2.1.1 Familiarity

The lived experience of HCV constructed by participants in this study was characterised by both striking familiarity, and more novel and original insight. The familiarity stemmed from recognisable and longstanding refrains which have dominated previous research in this area, and which continued to permeate these contemporary themes. For example, socio-culturally mediated reactions to a HCV diagnosis during the era of DAAs suggested an improving cure had done little to lessen the emotional impact of infection. Participants described responses aligning with the shock, fear and depression which typified previous research conducted during the interferon era (Glacken *et al*, 2001; Groessl *et al*, 2008; Olsen *et al*, 2012; Sgorbini *et al*, 2009; Sutton and Treloar, 2007). Similarly, discussion of the uncertainty of life with HCV, and the enduring and consuming emotional burden of infection also echo findings from previous studies. Uncertainty has long been explored as an important facet of the experience of being HCV positive (Conrad *et al*, 2006; Hill *et al*, 2015; Rhodes and Treloar, 2008), and the tenacious hold which stigma exerted over the participants' lives resonated with accounts of discrimination and prejudice from previously published works (Butt *et al*, 2008; Conrad *et al*, 2006; Faye and Irurita, 2003; Fraser and Treloar, 2006).

The importance of these resilient themes to contemporary narratives lies in their exposition of the lack of influence a rapidly improving cure has yet to exert on the emotional burden of illness. The fact that enduring motifs of stigma and distressing uncertainty remained a fundamental component of the participants' realities, speaks of how the 'medical triumph' (Chung and Baumert, 2014) of HCV treatment has yet to influence significant domains of the participants' lives. The cultural memory of what it means to be HCV positive persists. This finding exposes how the advances witnessed in HCV therapy, and the lived experience of being HCV positive, appear in many ways detached and isolated from one another. Improvements in one, do not necessarily

equate with improvements in the other. Academic, scientific and medical attention on treating and curing the somatic disease has decontextualised HCV from peoples' lives, priorities and realities. It has largely failed to concurrently address those aspects of living with HCV which the participants constructed as most significant and detrimental to their wellbeing. A medical focus on rapidly improving therapeutic options, has sidelined an emphasis on person-centred care, and disregarded the psychosocial sphere within which the burden of illness is most keenly felt. This study highlights domains of the HCV illness experience which have so far proved immune and unyielding to this new era of therapy. However, that is not to say that the advances in HCV treatment did not impact on participants' lives at all. Indeed, whilst a familiarity pervaded many aspects of the participants' testimonies, the preceding chapters have demonstrated that fresh and novel insights into the lived experience of HCV were also established.

These novel insights were underpinned by the manner in which developments in drug therapy were understood and articulated by the participants. It is therefore necessary to reflect on how these understandings were formed. The majority of participants in this study were accessing specialist care for the management of their HCV infection, to a greater or lesser extent. As the way humans classify and attach meaning to the outside world is not a purely individual process, and understandings of disease are shaped in part by the perceptions of others, this interaction with healthcare professionals had significant influence on the participants' comprehension of HCV and its treatment. The prevailing discourse from the healthcare team, and the manner in which they framed the developments in HCV drug therapy, contributed to how participants contextualised their experience of living with the virus.

8.2.1.2 Treatment rationing

The inequality of access to new HCV treatments encountered by participants during the study had considerable influence on their experience of the disease. The shifting eligibility criteria for accessing DAA regimens (HIS and NHS National Services Scotland, 2015a; 2015b; Scottish Government, 2015b) created the conditions for many of the key thematic findings within this study to become established. For example, an understanding of how treatment eligibility could be connected to liver health, gave rise to uncertainty in the participants about their access to such therapies, and reinforced

existing uncertainty related to liver disease progression. Treatment rationing also fractured the understanding of HCV as a singular disease. Individuals positioned themselves as more or less deserving of treatment than others, strengthening a perception that receiving such therapies was an honour and a privilege, rather than a right.

This inter-thematic discourse illustrates how implicit acceptance of the health inequality status quo underpinned the participants' experience of being HCV positive. The participants constructed narratives around the assumption that HCV treatment rationing was an absolute, and adapted their outlook and understanding to accommodate that assumption, rather than challenge it. This instinctive tolerance of health injustice speaks to theoretical arguments which suggest that an individuals' capability to be healthy can be constrained by their physical and social environments, as well as the political, economic, cultural and legal determinants of those environments (Venkatapuram, 2011). The participants' implicit acceptance of treatment rationing emphasises the lack of moral entitlement to health felt amongst this group of disenfranchised individuals, and further, the lack of capacity to achieve a state of wellbeing. This finding resonates with the lack of entitlement and tolerance of rights violations which have been reported within HCV communities over the years (Wolfe *et al*, 2015), and underscores the lack of entitlement to therapeutic citizenship felt amongst the participants (Rhodes *et al*, 2013). It exposes how treatment guidelines which emphasise disparity of access serve only to reinforce notions of discrimination and prejudice, further marginalising and stigmatising already marginalised and stigmatised groups. Indeed, the subtext of treatment rationing, implying some are undeserving or unworthy of care, becomes explicit when the sustained and tenacious influence of internalised stigma on the participants' lives is considered. It is perhaps unsurprising that participants continued to feel dirty, ashamed, and to blame for an infection that their providers may not always deign to treat.

Of course, the issue of rationing is not unique to the treatment of HCV. A cursory literature search reveals recent articles pertaining to rationing in fields as diverse as palliative care (O'Connor and Casarett, 2016), surgical interventions (Orchard, Wright,

Kelly, McCabe and Hewes, 2016; Owen-Smith, Donovan and Coast, 2016) and drug resistant tuberculosis (Martin *et al*, 2016). The rationing of treatment has been argued as an inevitable consequence of medical advances (ter Meulen, 2008), and global ethical and economic debate surrounding distributive justice and treatment rationing permeate medical and academic discourse (e.g. Carter, Gordon and Watt, 2016; Fleck, 2016; Scheunemann and White, 2011). In light of such complex arguments, merely stating that the rationing of HCV treatments is detrimental to those living with the infection and should therefore be abolished would be simplistic and naïve. However, this study *does* add to the growing dialogue by demonstrating how this scholarly debate is firmly embedded within the lived experience of HCV positive individuals. For participants accessing care, the inequality of treatment was a tangible and fundamental factor underpinning multiple aspects of their daily life, rather than just an academic concern.

One further consideration with regard to treatment rationing is how this relates to the global reconstruction of HCV as a public health priority. The two processes appear ill at ease. The significance of highlighting HCV as an international public health challenge, comparable to tuberculosis, HIV and malaria (World Health Assembly, 2016), is weakened and undermined by a response from care providers which could often position treatment as a future consideration. The inequality of access to treatment in this study supported an opinion amongst the participants that HCV need not always be an immediate concern. For some, liver disease was mild and insignificant therefore treatment could be safely deferred to a later date. Whilst this discourse served to strengthen arguments for treatment rationing, it also clashes with the urgency and precedence invoked by axioms such as '*major public health threat*' (Public Health England, 2016, p.1), and framings of HCV as 'deadly' and a 'time-bomb' in the popular press (BBC, 2009; Johnston, 2014). Treatment rationing confuses and blurs the constructed identity of HCV as a public health priority, and may threaten its authority amongst those infected with the virus.

8.2.2 Question two

“How adequate do theories of chronic illness remain to the contextual understanding of the experience of living with HCV?”

8.2.2.1 Theories of chronic illness

Previous studies conducted during the interferon era have drawn on a variety of sociological theories of chronic illness to illuminate their findings (Glacken *et al*, 2001; Hill *et al*, 2015; Olsen *et al*, 2012; Paterson *et al*, 2006; Sutton and Treloar, 2007). Predominant amongst these have been Bury’s (1982) theory of chronic illness as biographical disruption, and Paterson’s (2001; 2003) model of shifting perspectives. Bury (1982) posits that a diagnosis of chronic illness can lead to the disruption of an expected life biography, and necessitate a renegotiation and reformulation of one’s self-identity. He described three aspects of disruption to the unfolding chronic illness: disruption of taken-for-granted assumptions and behaviours; disruption in explanatory systems; and finally, the response to this disruption. In doing so, he conceived a process of accommodation to the disruptive event, which resulted in an altered life trajectory with some acceptance of the disease. He notes:

“...chronic illness involves a recognition of the worlds of pain and suffering, possibly even death, which are normally seen as distant possibilities or the plight of others (...) Further, the expectations and plans that individuals hold for the future have to be re-examined”

(Bury, 1982 p.169)

In contrast, Paterson’s (2001; 2003) model of shifting perspectives opposes such an end-goal conception, theorising living with a chronic-illness as an on-going process, in which people experience a complex dialectic between themselves and the world. The model illustrates how perceptions of chronic illness contain the dual perspectives of illness and wellness, with each of these perspectives alternately taking the foreground, dependent on people’s needs and situations.

In order for such theories to remain relevant to contemporary narratives, the construction of HCV as a long-term condition must endure. In previous research,

socially mediated notions of HCV chronicity have been repeatedly tied to the poor tolerability and efficacy of treatments available at the time (Fraenkel *et al*, 2005; Groessl *et al*, 2008; Hill *et al*, 2015; Kinder, 2009; North *et al*, 2014; Swan *et al*, 2010), in addition to a lack of information relating to the virus (Fry and Bates, 2012; Glacken *et al*, 2001; Groessl *et al*, 2008; Jiwani *et al*, 2013; Roy *et al*, 2007; Tompkins *et al*, 2005). Whilst these factors persist in many regions of the world, the political and economic response to HCV in Scotland has created an environment which may have challenged these notions. Although rationed, access to highly effective and tolerable HCV therapies has been granted for many with the infection (HIS and NHS National Service Scotland, 2015), and a strategic framework raising awareness of HCV at a population level has been in place for over ten years (Scottish Executive, 2006; Scottish Government, 2008; 2011; 2015a). Did perceptions of socially produced chronicity therefore still hold true for the participants in this study? Indeed, is continuing to contextualise HCV as a chronic condition a misnomer given how readily it can now be eradicated for those accessing treatment?

8.2.2.2 Chronicity within the themes

To answer these questions, it is necessary to reflect on how an overarching discourse of disease progression and HCV chronicity were woven throughout the themes. The narrative of positioning HCV was underpinned by an assumption that it was not a static and unchanging entity, but an advancing threat which could ultimately get worse over time. The discourse of participants feeling fortunate, and favourably comparing themselves to others with the disease, was only possible if HCV was understood as an unequal illness, with degrees of severity and diverse trajectories. The foundations of 'positioning HCV' rest on the participants' often implicit acknowledgement that they were at a particular point along an illness continuum: that HCV could progress and become more debilitating, and potentially life-threatening, in the future.

Of course, participants' understanding of HCV as a progressive disease with long-term implications, does not automatically equate with a notion that they expected to remain HCV positive, and move along that illness continuum. There is a difference between constructing HCV as a *potentially* chronic and debilitating condition, and perceiving that such long-term effects will be directly experienced. Hepatitis C is, after

all, curable for the majority of those who complete a period of treatment, and as previously stated, most participants in this study were already accessing specialised HCV care. Was acknowledgement of disease progression therefore solely a discursive positioning strategy, used protectively to emphasise the participants own perceived good fortune? Consideration of the discourse emphasising the emotional strain of living with HCV suggests not. The persistent unease and emotional burden which were integral to the experience of being HCV positive were fed by multiple worries, which included the inability to self-monitor the effects of HCV, and related fears of long-term disease progression. The progressive nature of HCV infection did not therefore constitute part of an improbable and unlikely illness trajectory, alluded to but ultimately disregarded. Rather, it established a very tangible recognition in the participants that they may experience the effects of advancing liver disease at first-hand. The emotional burden of infection illuminates how the existence of an effective, and well-tolerated cure, did little to calm anxieties over the potential long-term implications of HCV, or negate the perception that the disease may prove a chronic concern.

Why the arrival of effective, well-tolerated treatments for HCV did not appear to have effectively challenged socially mediated notions of chronicity is intriguing. Previous discussion of treatment rationing could be presumed to play a considerable part, in addition to the lack of impact these therapies wielded in crucial domains of the lived experience. However, the data also reveal more nuanced contributory factors, such as the manner in which participants articulated their understanding of the nature of these therapies. These effective, well-tolerated regimens, feted and lionised within medical discourse (Chung and Baumert, 2014; Pawlotsky *et al*, 2015a) were not met with the same chorus of adoration by the study participants. Rather, a discourse of uncertainty and confusion emerged, emphasising a vague understanding and ambiguous grasp of HCV treatment evolution. This uncertainty may have been actively maintained as a coping strategy (section 6.5.1) nevertheless, its presence provides further insight into why an infection that now achieves a cure in over 90% of those taking treatment, continued to be framed as a chronic disease. Understandings of new treatments were too insubstantial and remote to challenge deeply-rooted beliefs forged in the interferon era, and perceptions of a progressive, long-term illness

persisted. How long this situation may endure is unknown. Within high-income nations, cultural memory of the interferon-based therapy era will naturally fade as the costs of interferon-free treatments reduce, and their use proliferates. In the short- to medium-term however, theories of chronic illness remain integral to illuminating the experience of those living with HCV, and the paradox of chronic illness models, for an increasingly curable disease, continues.

8.2.3 Question three

How is interferon-free treatment for hepatitis C experienced and contextualised?

8.2.3.1 The legacy of interferon

The exploration of undertaking interferon-free therapy in this study emphasises how the participants' prevailing discourse was informed by an awareness of treatment during the interferon era. Interferon-free regimens were not solely appraised, considered and experienced on their own merits, but in the context of previous standards of care. Treatment of HCV during the interferon era was characterised by a range of physical and psychological side-effects, whose severity and persistence perniciously impacted on self-identity, social interaction and relationships with family and friends (Fraenkel *et al*, 2006; Hopwood and Treloar, 2005; Janke *et al*, 2008; Kinder, 2009; Sgorbini *et al*, 2009; Sheppard and Hubbert, 2006; Taylor-Young and Hildebrandt, 2009; Zickmund *et al*, 2006). The participants' experience of interferon-free regimens in this study was intricately tied to this historical touchstone, with the legacy of interferon underpinning and shaping their discourse. For example, discussion of side-effects continued to dominate the participants' narratives. However, whilst the burden and severity of these ailments had been the historical focus of concern, it was disbelief at the relative *absence* of such side-effects which now took precedence in their accounts.

8.2.3.2 A cultural lag

The disparity between underpinning expectations of interferon-free treatments and the participants' subsequent experience of them illuminates a cultural lag between the rapid pharmacological developments which have been witnessed, and the social

understanding of them. Ogburn's (1922) durable theory of cultural lag suggests that this societal phenomenon exists when swift advances in material culture (such as new technologies or therapeutic developments) are not matched by equally swift cultural adaptation to such innovations. As a result, a period of maladjustment occurs, when non-material culture struggles to adapt to new material conditions (Schaefer, 2012). The findings from this study suggest that such a period of maladjustment is currently being witnessed with regard to new HCV therapies, offering insight into how these treatments are experienced, but also articulating with previous discussions of chronicity and the persistence of resilient themes for those living with the virus. The societal adjustment to a new era of HCV therapy trails behind the observed pharmacological advances.

8.3 Limitations of the study

Prior to considering the implications of this thesis, it is necessary to focus attention on the limitations of the study. Limitations have the potential to affect the quality of the findings, and may restrict the transferability of those findings to other settings. Pragmatic consideration of conceivable limitations therefore contributes to the rigour and credibility of the work.

8.3.1 Personal limitations

The most obvious limitation within any doctoral study, must be the ability of the doctoral student themselves i.e. my own aptitude and capacity for conducting the work. The common description of a PhD as a period of training, aimed at developing and honing research skills (Petre and Rugg, 2010), underlines that this thesis is not the work of an experienced and expert researcher, but that of a novice trainee. The very nature of a doctoral study therefore presents possible limitations to the quality of the findings. For example, I interviewed the participants, coded the data and developed the analytical narrative, despite never having attempted these tasks previously. Whilst my own inexperience may therefore cast doubt on the credibility of the work, the nature of a doctoral study also demands supervisory expertise, which seeks to counter such concerns. This supervisory expertise was present from the conception of the study, and throughout the planning and completion of the work. Frequent meetings with the full supervisory team sought to review, challenge and interrogate multiple

aspects of the research design, data generation and the developing analysis. Such regular and robust feedback created an instructive and supportive learning environment, in which my limitations as a novice researcher were recognised, appropriately addressed and, hopefully, adequately overcome.

In addition to my inexperience as a qualitative researcher, my previous role as a HCV nurse specialist also posed potential limitations to practical aspects of recruitment and data generation. For example, as I was well-known to the healthcare team within the main recruitment site, some members of that team unintentionally limited my access to potential participants through a wish to make my research journey as smooth and straightforward as possible. Soon after the inception of the study, I noted a reluctance of some staff to approach potential participants who they considered insufficiently verbose, unreliable or too chaotic to trouble me with. A well-intentioned desire for me to succeed with my research was inadvertently making that outcome less likely. I hadn't fully appreciated the impact so-called 'gatekeepers' would have on my ability to recruit the diverse sample of participants I had planned, but these individuals' own idiosyncratic sampling strategies proved a major barrier to enrolling people in the study in its early stages. To avoid alienating myself from the team, challenging this required a tactful and diplomatic approach. However, by liaising with staff on a one-to-one basis, and explaining the aims of my research in greater detail, some headway was quickly made, and a broader range of potential participants were gradually referred.

My interview technique was, at times, also limited by my previous professional experience. Reflective readings of the interview transcripts illustrated how prior familiarity with some of the participants' discourse resulted in a failure to always prompt for richer data. Anecdotes were prefixed with assertions of "*you know it yourself*" or "*you know what it's like Dave*"⁴³, to which I found I sporadically concurred, rather than seeking deeper insight from the participant's perspective. The concept of bracketing in social phenomenology demands the suspension of belief in the world as I know it (Levesque-Lopman, 1988), yet demonstrations of my own unquestioning

⁴³ Keith, 54, known to me from my clinical role prior to the study

acceptance in what I thought I knew intermittently appeared within the data. Whilst clearly a limitation of the study and an area for further personal development, reflecting on the transcripts throughout the process of data generation helped to improve and sharpen my phenomenological technique for subsequent interviews. The iterative nature of data generation and analysis therefore helped to ameliorate the impact of this limitation to the study.

8.3.2 Methodological limitations

In addition to the inexperience of the researcher, a common limitation levelled at research underpinned by a phenomenological methodology, is to what extent the work aims to illuminate the phenomenon in general (as an experience shared by many), or focus on more idiographic understandings of individual experience, eschewing broader insights (Finlay, 2009)? The importance of this question lies in the transferability of a study's findings to other settings, which contributes to the overall rigour and trustworthiness of the endeavour (Morse, 2015). By adopting a social phenomenological perspective, the aim of this study was to explore the commonalities found in the inter-subjective experience of being HCV positive, and the analytical techniques employed served to achieve this goal. However, the commonalities (themes) revealed within this thesis are those constructed by analysis of the narratives of these particular study participants, and in order to consider the limits of transferability, the composition, setting and socio-political contexts of those participants must be reflected on (Polit and Beck, 2010).

The purposive sample of study participants were all drawn from one geographical region of Scotland, and from one Health Board area. The maximum variation sampling strategy aimed to produce a high degree of variation amongst these participants (section 3.4.1.1). However, recruiting individuals who were not engaged with HCV care proved more problematic than had been anticipated (table 3, p.77). The principle reason for this lay in the difficulty of maintaining productive and fruitful relationships with multiple recruitment sites spread over a wide area. Although staff in various recruitment locations were supportive of the study, the demands of their daily workload and my inconsistent presence at the sites contributed to a lack of impetus in identifying potential participants. This group were also particularly inconsistent in

their attendance at the recruitment locations, and often unreachable by phone, which resulted in numerous missed opportunities to engage. The result of these difficulties was a sample composed predominantly of individuals who were already engaged with specialist HCV services to a greater or lesser extent⁴⁴, and as such may represent a fairly restricted population. The latest figures available estimate 28% of those diagnosed with HCV in Scotland attended a specialist centre for care in 2014 (Public Health England, 2015), therefore caution should be exercised when relating these findings to those infected with HCV more generally.

The scarcity of participants who did not engage with HCV services, also contributed to the relative dearth of those who identified as active PWID in the sample. Whilst this restricted the comparative potential of the data, and limits the transferability of the findings, this research project was never intended to focus primarily on individuals who reported ongoing injecting drug use (table 3, p.77). Previous studies suggest that the experience of living with HCV for this group of individuals differs markedly from those who identify as previous PWID, and those who have no drug-using history at all (Copeland, 2004; Davis and Rhodes, 2004; Harris, 2009; Wozniak *et al*, 2007). As such, a specific contemporary investigation focused on current PWID, would serve to illuminate the influence an evolving era of HCV drug therapy may be having on their experience of living with the disease. Recent academic discussion of the benefits of pursuing HCV treatment as prevention (TasP) strategies amongst this population would make this a particularly relevant and enlightening endeavour (Harris *et al*, 2015; Hickman, De Angelis, Vickerman, Hutchison and Martin, 2015).

Finally, the Scottish setting of this study should also be considered within this discussion of limitations. Globally, national strategies to address the HCV epidemic demonstrate considerable variation, with Scotland frequently acknowledged as leading the way in tackling the disease (Ulmer and Hughes, 2013) alongside other high-income nations such as Australia (Australian Government, 2014). Whilst world-leading, the Scottish experience of a nationally coordinated action plan, and regulated access to new medications differs vastly from the current situation in low- and middle-income

⁴⁴ The two study participants who were not engaged with specialist care, Eilidh and Dean, were recruited through a GP practice with the aid of a particularly motivated and dynamic GP.

countries (Graham and Swan, 2015) where the global burden of infection is predominantly felt (Mohd Hanafiah *et al*, 2013). The findings from this study are located within a particular socio-political context which should not be overgeneralised.

8.4 Implications of the study

The obvious question which arises from this exploration into the contemporary lived experience of HCV is why does it matter? The purpose of health-related social science research is ultimately to inform action, and therefore consideration of how the findings from this study connect with strategy, service delivery and frontline care must be made. What implications does this work have when considered within the contexts of policy aimed at addressing the HCV epidemic, the strategic delivery of treatment and the clinical practice of those working with HCV positive individuals on a daily basis?

8.4.1 Implications for policy

Within Scotland, the strategic framework for addressing HCV originated in a two phase action plan launched in 2006 (Scottish Executive, 2006; Scottish Government, 2008). This action plan was later subsumed into a national framework with a broader remit, addressing sexual health and blood borne viruses in an integrated, cross-agenda approach (Scottish Government 2011). The framework is guided by five high-level outcomes, of which four connect directly to HCV:

Outcome 1: Fewer newly acquired hepatitis C infections.

Outcome 2: A reduction in the health inequalities associated with hepatitis C.

Outcome 3: People affected by hepatitis C lead longer, healthier lives.

Outcome 5: A society whereby the attitudes of individuals, the public, professionals and the media in Scotland towards hepatitis C are positive, non-stigmatising and supportive.

(Scottish Government, 2011, p.32)

These outcomes are based on key aims identified in the second phase of the original HCV action plan (Scottish Government, 2008), and as such, are firmly rooted in the interferon-era. Whilst much progress has been reported in addressing these objectives

(Scottish Government, 2015a), the findings from this research cast doubt on whether they remain collectively achievable, and fit for purpose, in a new age of therapy. The significant influence of treatment rationing on the experience of living with HCV, implies the stated outcomes are contradictory and no longer compatible with each other. For example, the prioritisation of treatment to those with a greater degree of liver disease (advocated within the 2015 framework update [Scottish Government, 2015a]) serves to work towards the realisation of outcome three. However, in doing so, it creates and imposes an array of *new* health inequalities associated with HCV, in direct opposition to outcome two. In addition, the acceptance and tolerance of those inequalities, evident throughout the participants' narratives, reinforces discrimination and stigma which sits uneasily alongside outcome five. Within the context of a new therapeutic era, this research implies these outcomes are mutually exclusive, rather than parts of a unified whole. The strategies in place to address particular outcomes are actively working against the realisation of others.

8.4.2 Implications for treatment delivery

The cultural lag exposed by this study has implications for how novel HCV treatments are delivered in clinical practice. It creates conflict between what patients *ought* to need during periods of therapy with interferon-free regimens, and what they actually require. All participants in this study, who commenced a period of therapy, received their treatment through a hospital-based clinic. However, moving therapy away from secondary care and into more diverse settings is now a key priority in Scotland (Scottish Government, 2015a), and there is an emerging evidence base to support that objective (Alavi *et al*, 2013; Brew, Butt and Wright, 2013). Interferon-based treatments have been successfully delivered in opioid substitution settings and prisons, achieving comparable adherence and response rates to those reported in more conventional locations (Grebely *et al*, 2016; Litwin *et al*, 2009; Rice *et al*, 2012). However, these support-intensive models of treatment delivery may be reviewed in light of fewer perceived patient requirements with 'easier' drugs. As interferon-free (and increasingly ribavirin-free) treatments proliferate, the clinical need for close haematological and side-effect monitoring of patients recedes (Lam *et al*, 2015), yet the significance of knowing the treatment to be working, and the continued

importance of support for individuals with significant histories of drug use and drug treatment are key findings within this study.

Global HCV discourse tends to focus on improving SVR rates, reduced side-effect profiles and decreasing treatment times (Asselah *et al*, 2016; Chung and Baumert, 2014; Pawlotsky *et al*, 2015a), yet understanding what motivates and reassures individuals whilst taking the drugs is essential in ensuring improved adherence and integral to interferon-free treatments reaching their full potential. In the often quoted words of former US Surgeon General C. Everett Koop “*drugs don’t work in patients who don’t take them*” (Osterberg and Blaschke, 2005). The cultural lag observed within this study suggests caution should be exercised in any reconsideration of how best to deliver interferon-free therapies to patients, as the experience of interferon-free treatment continues to demonstrate a significant and essential discourse of needs. This finding could also have implications for the large-scale implementation of HCV TasP initiatives, which whilst theoretically possible (Hickman *et al*, 2015), have yet to be empirically tested.

8.4.3 Implications for practice

Discussion of treatment delivery emphasises how the care of individuals with HCV is governed by an acute focus on curing the disease. This acute care model positions those with HCV as patients who receive expert advice from healthcare practitioners, rather than informed individuals who live, and have lived, with the disease on a daily basis. It also perpetuates common assumptions about acute illness, for example that it should be the patient’s predominant concern and highly prioritised (Paterson *et al*, 2006). Such a model concentrates on disease process, symptom management and viral eradication, whereas the findings from this study suggest the burden of HCV infection is felt in much wider social and emotional contexts, which often remain unrecognised and unaddressed. The acute model of HCV care is attentive to physical manifestations of disease, yet much of the burden of illness appears psychogenic and social in nature.

Acute models of care also clash with the enduring perception of HCV as a chronic condition for those living with the virus (Paterson *et al*, 2006). Despite improving

therapies, the understanding of HCV as a long-term concern continued to underpin the discourse of participants in this study. This discord, between acute care and chronic disease, may result in patients and healthcare practitioners harbouring competing agendas, potentially undermining the therapeutic relationship by negatively impacting on patient-provider interactions (Haworth and Dluhy, 2001). The findings from this study imply an acute model of care fails to address the experience of living with HCV. An overriding emphasis on treatment ignores the broader meaning of HCV in the lives of the individuals affected, and fails to tackle key anxieties and concerns. A more person-centred approach to HCV care is needed, if the true burden of illness is to be confronted.

8.5 Recommendations

The findings and implications of this work give rise to a number of recommendations for policy, future research and clinical practice. Discussion of these recommendations aims to demonstrate how this thesis offers practical application at a range of different levels, and to a variety of stakeholders.

8.5.1 Recommendations for policy

As previously stated, the findings from this thesis suggest that the key aims of the strategic framework for addressing HCV in Scotland are no longer compatible in a new era of treatment. As such, a critical review of the existing *Sexual Health and Blood Borne Virus Framework* (Scottish Government, 2011; 2015a) and how it relates to the contemporary experience of HCV should be made. A practicable and relevant framework is essential in guiding governmental responses towards the elimination of HCV as a public health threat by 2030 (Hepatitis B and C Public Policy Association, 2016; World Health Assembly, 2016).

In addition, this study has emphasised how stigma continued to exert a pervasive and obstinate influence on the lives of the participants. The reduction of stigma is stated as a key outcome within the existing *Sexual Health and Blood Borne Virus Framework* (Scottish Government, 2011), and whilst the Ministerial foreword to the 2015 update celebrates being “*proud of our bold commitment to challenge stigma in all its forms*” (Scottish Government, 2015a, p.2), the document itself fails to report any HCV-specific

progress on this. Indeed, discussion of stigma is entirely absent from the section of report dealing with viral hepatitis, with the identification of key developments since 2011, and key priorities up to 2020, making no reference to stigma whatsoever. It is therefore necessary for governmental policy to pay more than lip-service to HCV stigma reduction, and initiate specific interventions with measureable outcomes to begin to address the problem. A government funded nationwide intervention has been initiated within the framework focused on the stigma and discrimination of individuals with HIV (Waverley Care, 2012), and a comparable approach for HCV should also be employed.

Of course, it is not solely HCV-specific policy which is of relevance to the lives of those afflicted by the disease. The burden of HCV in Scotland is associated with deprivation and substance use, and predominantly located within some of the most vulnerable and disenfranchised sections of society (Scottish Government, 2011). This thesis has underscored how the implicit acceptance of health inequalities was integral to the experience of the participants, which speaks of how their capability to be healthy was fundamentally constrained (Venkatapuram, 2011). As such, it is recommended that the *Sexual Health and Blood Borne Virus Framework* is not progressed in isolation, but forms strategic links with other governmental schemes and policies which seek to address social determinants of health. Whilst it is acknowledged that this is a fairly broad and non-specific recommendation, an insular focus on the prevention, testing and treatment of HCV may disappoint, if the ability of HCV positive individuals to engage with that programme of care is constrained by their social environment (and its political determinants).

8.5.2 Recommendations for future research

The findings from this study also suggest areas where further academic research would be beneficial. This thesis presents a temporal snapshot of the lived experience of HCV and its treatment, offering valuable insight into how individuals understand and make sense of the disease. However, the context in which this study is located continues to evolve. As recurrently stated, the developments in HCV treatment are ongoing, and further interferon-free options for multiple HCV genotypes are set to become available within Scotland over the coming years (e.g. SMC, 2016). As the cultural memory of

interferon fades, additional qualitative research will be needed to allow comparable insight into the influence these continued pharmacological advances have on the experience of living with HCV.

Further, as previously discussed, this research is limited by the lack of active PWID recruited to the study. As the discourse of HCV TasP continues to gain more attention and authority (Cousien *et al*, 2016; Hickman *et al*, 2015; Leask and Dillon, 2016), understanding how HCV and its treatment are experienced by individuals actively injecting drugs gains greater significance. Theoretical discussion of scaling up HCV treatment among active PWID has so far failed to account for how these communities perceive this new era of therapy. The patient perspective appears to have been overlooked as irrelevant and inconsequential within the population-based rhetoric of HCV TasP (Harris *et al*, 2015). Contemporary qualitative research focused on the lived experience of HCV positive PWID is needed to inform empirical HCV TasP initiatives, and support them reaching their full potential.

8.5.3 Recommendations for clinical practice

Finally, the findings from this study also produce recommendations for clinical practice. The acute model of care which currently dominates service delivery largely fails to address the multiple social and emotional aspects of living with HCV, and disregards the ongoing construction of the disease as a chronic concern. The extent to which care can be characterised as ‘person-centred’ is therefore debatable. Whilst the treatment of HCV is an understandable and expected goal for care providers, this ultimate ambition should be embedded within holistic patterns of care which seek to treat not just the biological pathogen, but also the ongoing effects and consequences of the virus. As stated at the beginning of this thesis, the name HCV does not simply designate an invariant biological reality, and the care of individuals living with the virus should therefore entail more than a focus on virus removal. This recommendation is elucidated in the following personal reflection.

8.6 Concluding remarks

8.6.1 A personal reflection

I began this thesis by relating my personal interest in, and experience of, the field of HCV, and reflecting on how I perceived the medical and academic discourse surrounding improving HCV treatment to be marginalising the experience of those living with the disease (section 1.1.6). My ambition throughout this work has been to honour the voice of the HCV patients I nursed over the years, and give a scholarly platform to their contemporaries' experiences, understandings and insights in a new era of therapy. Whilst I hope the preceding chapters have realised that ambition, conducting this research study has also provided me with innumerable personal opportunities for learning and reflection. Each step in the research process has presented me with new challenges, from exploring theoretical debates into the nature of reality, to the more practical development of effective interviewing and analytical skills. Significantly, my three-year immersion in the research process has also compelled a timely re-examination of my own professional practice as a nurse, and forced me to question whether my avowed commitment to person-centred care has always been demonstrated in my actions. Whilst my intent to honour the voices of HCV positive individuals within this study is apparent, it has obliged me to interrogate the value I had previously placed on those voices within my own clinical practice.

It was during my second interview with Happy, one of the study participants, that this thought really took hold. When asked about her treatment experience, she described her most significant help during therapy as something disregarded and comparatively disparaged by the treatment team:

I wasn't asked about my lifestyle, I was asked about it but they seemed not to really pay any attention, to be not really seriously considered (...) it was more important to me. Like, when I said I was introducing to yoga, I wasn't asked about it, but it really really played a big role, because like with hot yoga, I was like sweating, so it was detoxifying the body, so for me I think that's what helped me...

(Happy, during her second interview)

Whilst reflecting on the interview afterwards, I queried whether my own reaction as a HCV nurse specialist would have been any different from that of the healthcare team

when confronted with Happy's idiosyncratic faith in the benefits of hot yoga. This anecdote made me question more broadly the value I had previously placed on patients' narratives in clinical consultations, and the gulf that can exist between the priorities and predominant concerns of HCV care providers, and those of individuals living with the virus. In hindsight, the mantra of viral eradication through effective treatment, which had always guided my clinical practice, had also been instrumental in necessitating a relative disregard for those aspects of living with HCV which may not affect, or seem peripheral to, the treatment pathway. I had heard the patient's voice when it spoke to my predetermined agenda, but turned down the volume when it spoke to theirs. Conducting this study has rebalanced my outlook between a clinical need for focused and directed treatment, and a care pathway which acknowledges and addresses those aspects of living with HCV which are most significant to the people concerned. The value of the patient perspective is not just an academic interest: it is a guiding principle for my future practice.

8.6.2 Thesis contribution

This study provides the first contemporary insights into the lived experience of HCV since the arrival of DAAs in clinical practice. It has illuminated what this new era of therapy means to individuals living with the virus, and exposed social and emotional spheres of illness, and a perception of illness chronicity, which remain untouched by the treatment revolution. Further, this work has emphasised that treatment inequalities are integral to how those with HCV articulate the disease, fundamentally underpinning multiple aspects of their daily lived experience.

This study also provides the first qualitative exploration of interferon-free treatments for HCV. It has revealed how the interferon legacy continues to cast a long shadow over the experience of interferon-free treatment, and exposed a cultural lag between the pharmacological advances currently being witnessed, and societal understandings and experiences of them. As such, it challenges notions of 'easier' therapy, and suggests the undemanding nature of these drugs may belie the challenges still faced in delivering these medications to the people who need them.

This thesis forms a timely addition to the global HCV discourse, which increasingly speculates on how improving therapies may lead to greater numbers of individuals accessing care, and potential global eradication of the virus. Such epidemiological conjecture often fails to account for how those living with HCV understand the illness, and the wider socio-political and cultural context within which treatment is undertaken. The individual, and their perception, beliefs and rights, are removed from the equation. This study has served to place the voice of those individuals back on the table, and underscore the importance of rich, vivid and recognisable insights to a contemporary understanding of living with hepatitis C.

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Appendix A

Journal publications resulting from this thesis prior to examination



Whiteley D., Elliott L., Cunningham-Burley S. & Whittaker A. (2015) Health-related quality of life for individuals with hepatitis C: a narrative review. *International Journal of Drug Policy*, 26(10), 936–949. doi: 10.1016/j.drugpo.2015.04.019

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Review

Health-Related Quality of Life for individuals with hepatitis C: A narrative review

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ABSTRACT

Background: The assessment of Health-Related Quality of Life (HRQoL) in hepatitis C (HCV) infected individuals continues to gain importance. However, rarely do reviews of this literature consider quantitative and qualitative accounts of HRQoL collectively, which only allows partial insight into the topic. This narrative review aims to address this gap in the literature.

Methods: Literature searches were conducted using seven databases with two separate search strategies, and results assessed for eligibility using specific inclusion/exclusion criteria; a data extraction sheet was used to identify the dominant themes for each research paradigm which were then distilled to key findings to construct the narrative.

Results: Quantitative investigation reveals a low HRQoL in individuals with HCV due to a complex multifactorial cause. During treatment for HCV, a further transient reduction is observed, followed by improvement if a sustained virological response is achieved. Qualitative data provide a recognisable voice to the everyday challenges experienced by individuals with HCV including insights into diagnosis and stigmatisation, contextualising how a reduced HRQoL is experienced day-to-day. Methodological limitations of these findings are then discussed. Much of the quantitative data has little relevance to current substance users as they are excluded from most trials, and appraisal of the qualitative literature reveals a marked difference in the lived experience of HCV infected current substance users and that of other HCV groups.

Conclusion: Concurrent analysis of quantitative and qualitative paradigms provides a deeper understanding of the true burden of HCV illness on HRQoL. Greater utilisation of qualitative research within international clinical guidelines is likely to be of benefit in identifying relevant HRQoL outcomes for substance users.

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Background

The latest reports estimate that worldwide between 130 and 150 million people are chronically infected with the hepatitis C virus (HCV), of which a significant number will go on to develop cirrhosis and hepatocellular carcinoma if left untreated (World Health Organisation, 2014). Within the UK, the most recent national estimates suggest around 214,000 individuals are infected (Public Health England, 2014), with injecting drug use continuing

to be the most common route of viral transmission (Palmateer et al., 2013). In recent years, dramatic advances have occurred in drug therapy for HCV with the arrival of Direct Acting Antivirals, a group of drugs which directly inhibit viral reproduction and have significantly improved treatment success rates (Conteduca, Sansonno, Russi, Pavone, & Dammacco, 2014). Despite this, treatment uptake remains low, with UK estimates of approximately only 3–5% of those infected accessing antiviral therapy (Public Health England, 2014).

With the historical move from a disease-centred model of medicine to a more biopsychosocial paradigm, a focus has emerged on not only the biomedical decrements of illness and curative benefits of treatment, but also the experience of illness and treatment from the patient perspective (Fayers & Machin, 2007); commonly termed ‘patient-reported outcome measures (PROMs)’.

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Increasingly, this focus is being given central importance in the planning of future healthcare improvements (e.g. *Scottish Government, 2010*) and the licencing of new medications (*Food & Drug Administration, 2009*), however PROMs are also used to inform clinical practice, aiding interaction and communication with patients and clients on a one-to-one basis (*Wu & Snyder, 2012*). Within the HCV research literature, the most commonly used quantitative PROM is Health-Related Quality of Life (HRQoL), a loosely defined term used to distinguish between aspects of life affected by disease or treatment for disease, and those broader quality of life issues such as access to green space within towns and cities (*Fayers & Machin, 2007*). HRQoL is ordinarily measured by standardised psychometric questionnaires, most commonly the 36-item Short Form Health Survey (SF-36) (*Ware & Sherbourne, 1992*), however there is no consensus on this survey's exclusive use within HCV research, and numerous other tools also appear within the literature. 'Patient-reported outcome measures' is an umbrella term used to encompass any report coming directly from a patient about their health condition or treatment however, and in this vein there is also a body of qualitative research which provides a more in-depth focus on HRQoL, by examining particular aspects of the lived experience (*Miller, McNally, Wallace, & Schlichthorst, 2012*). Arguably, these two bodies of research complement each other, with qualitative studies giving a recognisable voice to the decrements and improvements in HRQoL described in the quantitative work; however by their use of different methods and focus on different populations they may also generate distinct insights into different HRQoL perspectives.

Existing reviews of the evidence in this area tend to focus on either qualitative or quantitative research and thus provide partial insight into the topic (e.g. *Foster, 2009; Treloar & Rhodes, 2009*). *Miller et al. (2012)* did conduct a dual quantitative and qualitative systematic review of research published between 2000 and 2009, however did not compare the relative strengths and weaknesses of the findings produced by each paradigm and excluded interventional studies which contribute a large part of the quantitative literature in this area. The current review has been conducted to examine and synthesise the breadth of current research into HRQoL for people living with hepatitis C from both research paradigms.

Methods

The search strategy focused on seven databases; Medline, CINAHL, Embase, Cochrane Library, JBI CoNNECT+, PsycINFO and ASSIA. Two separate search strategies were developed to identify both quantitative and qualitative reports. For quantitative papers, comparable search terms for 'Hepatitis C', 'Health-Related Quality of Life' (including common abbreviated forms) and 'Patient Reported Outcomes' were used, accounting for variation in the Subject Index Terms specific to each search engine. For qualitative papers, comparable search terms for 'Hepatitis C', 'Quality of Life' or 'Life Experience' and 'Qualitative Research' or 'Interview' were used, again accounting for variation in specific Subject Index Terms (the term 'Quality of Life' being used more generally within the qualitative literature than the more specific HRQoL). In order to obtain papers that provided a detailed historical and contextual view as well as giving contemporary relevance, databases were searched to the extent of their temporal limits, preceding the publication announcing the isolation of HCV (*Choo et al., 1989*) in most cases. Table 1 provides an example of the electronic search strategy conducted. The search was not limited to only those papers which focused on HRQoL in HCV positive injecting drug users, as we sought to examine the comparative differences in HRQoL between this group and other HCV infected individuals, in addition to contrasting the way each research paradigm reveals

this. As the description of participants in studies varies (e.g. current injecting drug users, substance users, active injecting drug users, previous injecting drug users), often with little clarification of what these terms indicate, limiting the review by description of drug use status could also become specious and subjective. The generic term 'substance user' has been used within this review, except where injecting drug use is made explicit within the literature.

Inclusion and exclusion criteria

Fig. 1 displays the results for the quantitative search strategy. The initial inclusion/exclusion criteria used were as follows: inclusion criteria were adult participants, an English language abstract, and specific quantitative HCV HRQoL data provided. Excluded papers were those dealing solely with other liver disease aetiologies, no HRQoL-related data, and papers concentrating on those undergoing haemodialysis or liver transplant, as these articles focused primarily on the impact of those specific interventions which is not the emphasis of this review. Both observational and interventional studies were included, as were reviews at this initial stage. Duplicate entries for the same article appearing in multiple search engines were removed. One hundred and fifty one articles and 18 reviews were then recovered, including seven articles identified from reference lists. Once examination of the reference lists was complete, review articles were then excluded as primary data sources. The remaining retrieved articles were studied during which a further 30 papers were excluded for reasons shown in Fig. 1. All the remaining 121 papers have informed this review and the main findings from this body of work are presented here. Some of these references have not been further cited within the main text however for reasons of succinctness and economy. Full details of the 121 papers can be found in Supplementary file 1.

Supplementary material related to this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.drugpo.2015.04.019>.

Fig. 2 demonstrates results for the qualitative search strategy. The inclusion criteria were as follows: adult participants, an English language abstract, 'life experience' focus and qualitative data reported. Exclusion criteria remained the same as the quantitative search strategy, and duplicate entries for the same article appearing in multiple search engines were removed. Seventy three articles were then recovered, including five reviews and eleven articles identified from reference lists. Review articles were then excluded as primary data sources. The retrieved articles were studied during which eleven further exclusions were made for the reasons identified in Fig. 2. All the remaining 57 papers have informed this review and the main themes from this body of work are presented here. However, not all articles have been further cited within the main text, and full details are given of all references in Supplementary file 2. Records of all articles reviewed ($n = 178$) were stored and managed online using RefWorks for both search streams.

Supplementary material related to this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.drugpo.2015.04.019>.

Analysis

Data was extracted from each study by the lead author using a data extraction sheet which identified the author(s), date and source of publication, study design, key findings, limitations and recommendations, and inclusion of substance users. Using these data key dominant themes were identified for each research paradigm, which provided the foundation for the formulation of results and the synthesis of a coherent narrative. A narrative

Table 1

Example of the electronic search strategy used within the Medline database for both the quantitative and qualitative search strategies. No limits were applied, searches last conducted on 29.09.2014.

| Quantitative search strategy | Number of studies | Qualitative search strategy | Number of studies |
|--|-------------------|---|-------------------|
| Search Terms (ST) or Subject Index Terms (SIT) S1: Hepatitis C (SIT), OR Hepatitis C, Chronic (SIT) OR Hepatitis C (ST) | 66,420 | S1: Hepatitis C (SIT), OR Hepatitis C, Chronic (SIT) OR Hepatitis C (ST) AND Quality of Life (SIT) OR Quality of Life (ST) OR Life Change Events (SIT) OR Experience (ST) | 2248 |
| S2: Patient Outcome Assessment (SIT) OR Patient Reported Outcomes (ST) OR Quality of Life (SIT) OR Health-Related Quality of Life (ST) OR HRQL (ST) OR HR-QOL (ST) OR HRQOL (ST) | 65,897 | S2: Qualitative Research (SIT) OR Qualitative (ST) OR Interview, Psychological (SIT) OR Interview as Topic (SIT) OR Interview* (ST) | 348,448 |
| S3: S1 AND S2 | 319 | S3: S1 AND S2 | 133 |
| Application of initial inclusion/exclusion criteria | 136 | Application of initial inclusion/exclusion criteria | 43 |
| Further exclusions following retrieval of full articles | 121 | Further exclusions following retrieval of full articles | 36 |
| Number of studies excluding reviews | 106 | Number of studies excluding reviews | 34 |

approach was adopted because of the variation in study design. A narrative review summarises different primary studies into a comprehensive holistic overview of the topic, rather than addressing specific questions. Whilst narrative reviews are most commonly qualitative in nature, one of their strengths lies in drawing together the diverse understandings of a scholarly research topic (Jones, 2004) and therefore the approach fits this dual paradigm review well. The main themes identified in the literature for each paradigm will be explored in a chronological manner, with causal investigation and HRQoL before, during and after HCV therapy focused on from the quantitative literature first, followed by examination of qualitative research concentrating on the experience of diagnosis through to the experience of HCV therapy.

Results

Causal investigation: virus-related factors

The quantitative literature demonstrates HCV positive individuals have reduced HRQoL in comparison to healthy controls or population norms (Table 2) and goes on to investigate and debate the underlying cause for this. Foster, Goldin, and Thomas (1998)

reported reduced HRQoL in patients with HCV which could not be attributed to either the degree of liver disease, or association with a history of injecting drug use, concluding the decrement was attributable to HCV per se. Bonkovsky, Woolley, and the Consensus Interferon Study Group (1999) subsequently reported data from a large multi-centre drug trial which supported this hypothesis, concluding that HCV infection reduces HRQoL independent of comorbidities or factors associated with the virus. These studies spearheaded research in this area, and results from more recent observational studies give weight to the argument that viral factors contribute to HRQoL independent of host-factors (John-Baptiste et al., 2009; Strauss, Porto-Ferreira, Almeida-Neto, & Teixeira, 2014). Whilst the mechanism for this is still debated, evidence of viral replication within the central nervous system adds weight to the argument (Forton, Karayiannis, Mahmud, Taylor-Robinson, & Thomas, 2004).

It is unlikely that any one factor is solely responsible for reduced HRQoL however, and a complex multifactorial cause is a more likely explanation. Virus-related factors and associated extra-hepatic manifestations of HCV (such as cognitive impairment, fatigue and depression) compounded by host-related factors, psychiatric and medical co-morbidities and the effects of stigma, are all likely to be significant contributors (Häuser, Zimmer,

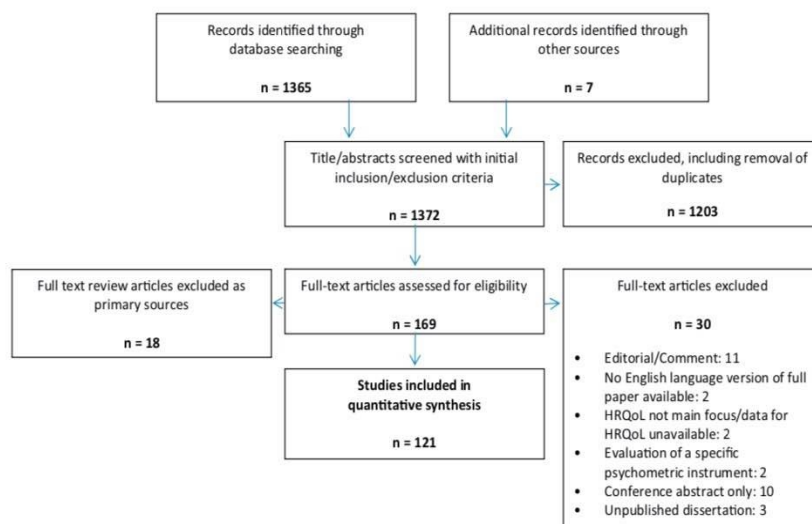


Fig. 1. Flowchart of included and excluded studies identified in the quantitative search strategy.

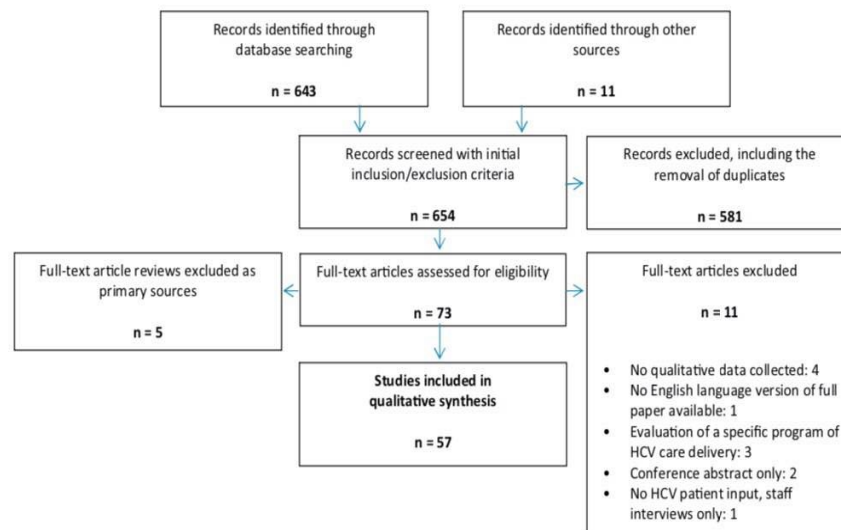


Fig. 2. Flowchart of included and excluded studies identified in the qualitative search strategy.

Schiedermaier, & Grandt, 2004; Helbling et al., 2008; Hsu et al., 2012). These will now be examined.

Causal investigation: host-related factors

The role of illicit substance use in relation to HRQoL decrements is an important consideration, given the high incidence of current or former substance users within this patient population (Hutchinson et al., 2006). Substance users experience a lower HRQoL than population norms irrespective of their HCV status (Dalgard, Egeland, Skaug, Vilimas, & Steen, 2004; Fischer, Conrad, Clavarino, Kemp, & Najman, 2013; Gjeruldsen, Loge, & Opjordsmoen, 2006; McDonald et al., 2013), and former substance users who acquired the infection through injecting drug use have been shown to have lower HRQoL than individuals who acquired HCV by another route (Foster et al., 1998; Hollander, Foster, & Weiland, 2006). Interestingly, a study by Dalgard et al. (2004) reported that active injecting drug users (IDUs) who believed they were infected with HCV had poorer HRQoL than those who did not or who did not know their status, irrespective of their actual serostatus, implying the knowledge (or assumed knowledge) of HCV positive status impacts HRQoL in addition to actually being infected with the virus. This echoes earlier work from a much smaller sample which found people who injected drugs, but were unaware of their HCV positive status had better HRQoL than those who were aware of their infection 26 years after being infected (Rodger, Jolley, Thompson, Lanigan, & Crofts, 1999). A recent much larger study from Scotland supports these findings. McDonald et al. (2013) assessed almost 3000 current IDUs accessing Injecting Equipment Provision Services in Scotland using the EQ-5D questionnaire and anonymised dried bloodspot testing, reporting a reduction in HRQoL between those who were aware of their HCV positive status and those who were not. Additionally, no difference in HRQoL was found between HCV negative IDUs and those who were HCV positive but unaware of their infection, supporting other work suggesting the impact of an undiagnosed HCV infection upon groups with already lower HRQoL than population norms places little additional burden, possibly due to the extent of co-morbidities present and overall lower HRQoL anyway (e.g. Schwarzsinger et al., 2004; Thein et al., 2006). In exploring the reasons for these findings however, it

becomes evident that the quantitative data available fails to provide sufficient insight. Why does undiagnosed HCV fail to impact on HRQoL for this population when it has been demonstrated to have a detrimental effect in other groups such as blood donors? (e.g. Strauss et al., 2014). Is the negative 'label' of HCV constructed around preconceptions about the chronic nature of the virus and its historically poor treatment outlook, or from external influences such as societal stigma? These points will be returned to in due course, when the qualitative literature surrounding the lived experience of HCV is examined.

In addition to substance use, other comorbid psychiatric and medical problems have also been implicated in reducing HRQoL in HCV patients (Hsu et al., 2012; Taliani et al., 2007). Häuser et al. (2004) argued that comorbidity is the best predictor of overall HRQoL reduction in patients with HCV, and further studies also highlight the importance of underlying medical and psychiatric comorbidities in reductions to both the mental health domains (Lim, Cronkite, Goldstein, & Cheung, 2006; Snow et al., 2010) and the physical domains (Kwan et al., 2008) of HRQoL assessment.

Causal investigation: stigma

As already described, substance users who were aware of their infection had lower HRQoL than those who were unaware (McDonald et al., 2013; Rodger et al., 1999) which may be due in part to the effects of stigmatisation towards these individuals which negatively affect their social status and self-image (Rodger et al., 1999). In one of the very few studies to combine a qualitative approach with a quantitative HRQoL assessment, Miller, Hiller, and Shaw (2001) described patients' distress by the perceived stigma associated with HCV, however without this qualitative adjunct the effect of stigma is poorly understood in the majority of HRQoL quantitative research.

HRQoL pre-treatment

The impairment in HRQoL for individuals with HCV has been shown to be equivalent to, or more severe than, the impact on physical and general health experienced by patients with other chronic conditions such as hypertension, type II diabetes, arthritis or depression (Bayliss et al., 1998; Bonkovsky et al., 1999; Kallman

Table 2

Summary of all studies identified within the quantitative search arm (see Supplementary file 1) where the most commonly used tool was employed (SF-36), and data reported for HCV patients versus 'healthy' controls or population norms in the 8 SF-36 subscales is available. 'S' indicates a reported statistically significant impairment compared with healthy controls or population norms.

| Author and year | n= | SF-36 subscales | | | | | | | |
|--|------|-------------------|---------------|-------------|----------------|----------|--------------------|----------------|---------------|
| | | Physical function | Role physical | Bodily pain | General health | Vitality | Social functioning | Role-emotional | Mental health |
| Bayliss et al. (1998) | 157 | S | S | S | S | S | S | S | S |
| Foster et al. (1998) | 72 | S | S | S | S | S | S | S | S |
| Bonkovsky et al. (1999) | 642 | S | S | S | S | S | S | S | S |
| Ware et al. (1999) | 324 | S | S | | S | S | S | | |
| Bianchi et al. (2000) | 126 | | S | | S | S | S | S | S |
| Fontana et al. (2001) | 107 | S | S | S | S | S | S | | S |
| Hussain et al. (2001) | 220 | S | S | S | S | S | S | S | S |
| McHutchison et al. (2001) | 912 | S | S | | S | S | S | | |
| Miller et al. (2001) | 95 | S | S | S | S | S | S | S | S |
| Kramer et al. (2002) | 100 | S | S | | S | S | S | S | S |
| Córdoba et al. (2003) | 120 | S | S | S | S | S | S | | |
| Gallegos-Orozco et al. (2003) | 157 | S | S | S | S | S | S | S | S |
| Dalgard et al. (2004) | 199 | S | S | S | S | S | S | S | S |
| Fleming et al. (2004) | 299 | S | S | S | S | S | S | S | S |
| Kang et al. (2005) | 182 | S | S | | S | S | | S | S |
| Kramer et al. (2005) | 120 | S | S | S | S | S | S | | S |
| Rowan et al. (2005) | 62 | S | S | | S | S | | S | |
| Balfour et al. (2006) | 123 | S | S | S | S | S | S | | S |
| Danoff et al. (2006) | 112 | S | S | S | S | S | S | S | S |
| Gjeruldsen et al. (2006) | 42 | S | S | | S | S | S | S | S |
| Hollander et al. (2006) | 147 | S | S | S | S | S | S | S | S |
| Lim et al. (2006) | 201 | | | | S | | S | S | S |
| Mathew et al. (2006) 'responders' | 25 | | | | | | | | |
| Mathew et al. (2006) 'non-responders' | 130 | S | S | S | S | S | S | S | S |
| Pojoga et al. (2006) | 35 | S | S | Excluded | S | S | S | S | S |
| Thein et al. (2006) | 267 | | | | S | | S | S | S |
| Bonkovsky et al. (2007) | 1144 | S | S | S | S | S | S | S | S |
| Kallman et al. (2007) | 130 | S | S | S | S | S | S | S | S |
| Taliani et al. (2007) 'non-responders' | 58 | S | S | S | S | S | S | S | S |
| Taliani et al. (2007) 'relapsers' | 43 | | S | | S | | S | S | |
| Taliani et al. (2007) 'untreated' | 163 | | | | S | S | | | |
| Teixeira et al. (2006) 'no liver biopsy' | 37 | | | S | S | | S | S | S |
| Teixeira et al. (2006) 'liver biopsy' | 40 | | S | S | S | S | S | S | S |
| Teixeira et al. (2006) 'for treatment' | 43 | S | S | S | S | S | S | S | S |
| Helbling et al. (2008) | 833 | S | S | S | S | S | S | S | S |
| Kwan et al. (2008) | 303 | S | S | S | S | S | S | S | S |
| Batki et al. (2009) | 100 | S | S | S | S | S | S | S | S |
| Björnsson et al. (2009) | 472 | | S | | S | S | S | S | S |
| Hsu et al. (2009) | 271 | S | S | S | S | S | S | S | S |
| Karaivazoglou et al. (2010) | 39 | S | S | S | S | S | S | S | S |
| Sinakos et al. (2010) | 99 | | S | | S | | S | S | |
| Chang et al. (2014) | 108 | | S | | S | S | S | S | S |
| Kuwashiro et al. (2014) | 175 | | | | S | | | | |
| Matsushita et al. (2014) | 228 | | S | | S | | | | |
| Strauss et al. (2014) | 35 | S | | S | S | S | S | S | S |

et al., 2007) and has more impact on physical domains than hepatitis B in mono-infection (Bondini et al., 2007; Foster et al., 1998) and in HIV co-infected individuals (Gillis et al., 2013). Of note, HCV also has a negative impact on mental health, an area in which detriments in other conditions are generally smaller (Foster, 2009; Tillmann et al., 2011).

A reduction in HRQoL can occur even in the absence of cirrhosis or significant liver disease (Bonkovsky et al., 1999; Córdoba et al., 2003; Foster et al., 1998; Häuser et al., 2004; Helbling et al., 2008; Rowan et al., 2005), and does not appear to be associated with Alanine Aminotransferase (ALT) levels (Arora et al., 2006; Foster et al., 1998; Helbling et al., 2008; Miller et al., 2001; von Wagner et al., 2006). Where advanced significant liver disease does occur however, further reductions in HRQoL are reported on a sliding continuum from advanced bridging fibrosis, to compensated cirrhosis to decompensation (Björnsson et al., 2009; Bonkovsky et al., 2007; Córdoba et al., 2003; Kallman et al., 2007; Snow et al., 2010). Although most HRQoL domains are affected, reductions in physical components are most frequently noted as being most sensitive to the negative impact of cirrhosis (Bayliss et al., 1998;

Bonkovsky et al., 2007; Córdoba et al., 2003; Kallman et al., 2007; Mandorfer et al., 2014). This low HRQoL in untreated HCV patients has been reported to have substantial economic costs to society, through loss of productivity, increased absenteeism from work and increased use of healthcare resources (El Khoury, Vietri, & Prajapati, 2012; Liu et al., 2012).

HRQoL during-treatment

The treatment of HCV has long been associated with a further transient reduction in HRQoL, largely attributed to the drugs used during therapy. For example, patients treated with Interferon- α (IFN) with or without ribavirin (RBV) demonstrated a significant increase in depression (Hunt et al., 1997), severe treatment-related distress (Bianchi et al., 2000) and a general decline in HRQoL during the period of therapy, which then returned to or surpassed baseline levels by 24 weeks post-treatment for those patients who achieved a Sustained Virological Response (SVR) (McHutchison et al., 2001; Ware, Bayliss, Mannocchia, Davis, & the International Hepatitis Interventional Therapy Group, 1999). With the pegylation of

interferon (PEG-IFN) a reduced impairment in HRQoL and less fatigue were reported during PEG-IFN and RBV therapy compared to IFN & RBV, especially in the initial 12–24 weeks, which had important implications for reducing treatment discontinuation (Bernstein, Kleinman, Barker, Revicki, & Green, 2002; Hassanein et al., 2004; Mathew, Peiffer, Rhoades, & McGarrity, 2006; Rasenack et al., 2003). The majority of these findings were from large multi-centre trials, however a similar pattern of transient decrement in HRQoL has also been described in observational cohorts (Hollander et al., 2006; Kang, Hwang, Lee, Chang, & Lee, 2005; Marcellin et al., 2011; Matsushita et al., 2014; Sinakos et al., 2010) and in HIV/HCV co-infection (Kemmer et al., 2012; Mandorfer et al., 2014; Thein et al., 2007).

With the arrival of Direct Acting Antivirals (DAAs), HRQoL data has begun to be reported timeously alongside biomedical end points. The polymerase inhibitor sofosbuvir was the first drug to have PEG-IFN free regimens reported in relation to HRQoL, which show significantly less impairment during therapy, although a modest decrement still remains during the 12 week treatment duration (Younossi, Stepanova, Henry, et al. 2014; Younossi, Stepanova, Nader, et al., 2014). As this data is exclusively from clinical trials it remains to be seen whether a similar scenario is observed in a patient population more representative of a typical clinical cohort; for example one including active substance users.

HRQoL post-treatment

For patients who achieve an SVR, benefits of treatment have been reflected in improvements to fatigue, and both physical and mental health domains of their HRQoL (Table 3). The domains in which improvements are reported are not consistent however, and indeed some studies have reported HRQoL remains significantly impaired following viral clearance with interferon therapy (e.g. Tillmann et al., 2011). With the differences between results from the reported studies, it is important to examine the various limitations that may have influenced these findings.

The time-point at which post-treatment HRQoL is measured could potentially influence the results obtained. For example, Pojoga, Dumitraşcu, Pascu, and Grigorescu (2006) concluded that antiviral therapy does not improve HRQoL, however their post-treatment measurement was taken immediately after therapy had finished. In contrast, a cross-sectional study by John-Baptiste et al. (2009) reported that patients who had achieved an SVR had improved HRQoL at an average of 3.7 years post-therapy. The majority of studies have measured for improvement in HRQoL at 24 weeks post end of treatment, a time when Helbling et al. (2008) note that the positive emotional response due to treatment success is still strong and possibly influences responses. More recently, measurement of SVR at week 12 post-treatment has been accepted as a primary end point for most clinical trials (Chen et al., 2013) with HRQoL data also collected at this time-point, possibly when the emotional response is even stronger, or the effects of treatment are still being felt.

Another frequently reported limitation in the literature is that of patient awareness of their serological result prior to completion of the psychometric tools; do patients *feel* better, simply because they know they have now cleared the infection? McHutchison et al. (2001) argued that as changes in HRQoL are seen in different domains and not reported 'across-the-board', it was unlikely that awareness of SVR was entirely responsible for the observed improvements. A later study which blinded serological results to patients and investigators found improvements in mental health for patients who had undetectable HCV RNA at week 12 of therapy compared to those who remained detectable (Quarantini et al.,

2008), supporting the theory that knowledge of cure cannot account for all HRQoL increases alone.

As shown, the quantitative literature deals primarily with HRQoL cause and effect, reducing the burden of illness to numeric estimates which may demonstrate statistical and clinical significance, but the true patient experience, and the patient voice, remains silent. It is with this in mind that we turn to the qualitative literature, and examine the main themes present in that body of work, beginning with the experience of diagnosis.

Diagnosis

A number of studies have drawn on the theory of chronic illness as biographical disruption (Bury, 1982) to provide insight into their participants' narratives of diagnosis. Medically, HCV is defined as a chronic infection if it does not spontaneously resolve within the first 6 months following acquisition (Seeff, 2002), however socially constructed chronicity refers to a state of long-term pain and suffering that may not be 'cured' (Martin & Peterson, 2009). For many, an initial reaction of shock was accompanied by overwhelming feelings of fear, denial, anger and depression following their HCV diagnosis (Glacken, Kernohan, & Coates, 2001; Groessl et al., 2008; Janke, McGraw, Garcia-Tsao, & Fraenkel, 2008; Olsen, Banwell, & Dance, 2012; Sgorbini, O'Brien, & Jackson, 2009; Sutton & Treloar, 2007; Tompkins, Wright, & Jones, 2005). Faye and Irurita (2003) describe their participants feeling condemned, with their futures being forfeited:

"It was a death sentence. Not knowing a lot about it, and asking my doctor if I was going to die in ten years and he couldn't tell me" (Faye & Irurita, 2003, p. 94)

In participants who had a history of injecting drug use, reactions to HCV diagnosis were sometimes modified and tempered, either because they suspected they were HCV positive anyway (Olsen et al., 2012; Temple-Smith, Gifford, & Stooë, 2004), or because of multiple HCV diagnoses within their peer group around the same time, providing context and mitigating the impact (Fry & Bates, 2012). It also served as an unwelcome reminder of a previous time in their lives, potentially exposing an earlier identity that many had worked hard to put behind them (Fry & Bates, 2012; Grundy & Beeching, 2004; Hill, Pfeil, Moore, & Richardson, 2014; Olsen et al., 2012):

"I was thrown right back there and it was awfully upsetting because I really did think that that time of my life was past and that I'd come to terms with grief and difficulty and all sorts of things in my life. And what happened? The legacy..." (Fry & Bates, 2012, p. 467)

For individuals who had been experiencing significant symptoms of HCV such as unexplained fatigue, the intensely negative reaction to their HCV diagnosis also came with a sense of relief as their health problems had finally been formally identified and medically labelled (Copeland, 2004; Glacken et al., 2001; Groessl et al., 2008). Importantly, the reaction of current IDUs to an HCV diagnosis appears to be significantly less traumatic; not conforming to Bury's (1982) notions and perhaps representing more 'biographical reinforcement' (Carricaburu & Pierret, 1995) than 'biographical disruption'. This will be discussed in greater detail in due course.

Following diagnosis, the re-evaluation of an individual's life and an attempt to regain control are commonly reported. Diagnosis can serve as a catalyst for the re-examination of life's priorities (Glacken et al., 2001), attempting to integrate HCV into a comfortable, acceptable and balanced future life (Faye & Irurita,

Table 3
Summary of all studies identified within the quantitative search arm (see Supplementary file 1) comparing HRQoL in HCV patients (as measured by SF-36 or HQLQ) who achieve SVR compared to their baseline levels or non-responders. Only studies where data for SF-36/HQLQ subscales has been reported are included. 'S' indicates a reported statistically significant improvement compared to baseline levels or non-responders. 'T' indicates a trend towards.

| Author and year | n= | Clinical trial data? | SF-36 subscales | | | | | | | | | | HQLQ additional domains | | | | |
|--|------|----------------------|----------------------|---------------|-------------|----------------|----------|--------------------|----------------|---------------|-----|-----|-------------------------|-----------------|---------------------|-----------------|---|
| | | | SF-36 summary scales | | | | | | | | | | Sleep | Health-distress | CHC health-distress | CHC limitations | |
| | | | Physical function | Role physical | Bodily pain | General health | Vitality | Social functioning | Role emotional | Mental health | PCS | MCS | | | | | |
| Bonkovsky et al. (1999) | 642 | ✓ | S | S | | S | S | S | | | | | | S | S | | S |
| Ware et al. (1999) | 324 | ✓ | | | | S | S | S | | | | | | | | | |
| McHutchison et al. (2001) | 912 | ✓ | S | S | | S | S | S | | | S | S | | | | | |
| Bernstein et al. (2002) | 1441 | ✓ | S | S | S | S | S | S | S | S | S | S | | | | | |
| Desnoor et al. (2003) | 168 | ✓ | S | S | S | S | S | S | S | S | S | S | | | | | |
| Rasnick et al. (2003) | 531 | ✓ | S | S | S | S | S | S | S | S | S | S | | | | | |
| Hassanain et al. (2004) | 1121 | ✓ | S | S | S | S | S | S | S | S | T | T | | | | | |
| Perrillo et al. (2004) | 412 | ✓ | | | | S | S | S | | S | | | | | | | |
| Kang et al. (2005) | 182 | ✓ | S | S | S | S | S | S | S | S | S | S | | | | | |
| Arora et al. (2006) | 491 | ✓ | S | S | S | S | S | S | S | S | S | S | | S | S | S | S |
| Bini and Mehandru (2006) | 92 | ✓ | S | S | S | S | S | S | S | S | S | S | | S | S | | |
| Dan et al. (2006) | 46 | ✓ | | | | S | S | S | | | | | | | | | |
| Hollander et al. (2006) | 271 | ✓ | | | | S | S | S | | | S | | | | | | |
| Matthew et al. (2006) | 147 | ✓ | | | | S | S | S | | | | | | | | | |
| Pujga et al. (2006) | 25 | ✓ | | | | S | T | | | | | | | | | | |
| Bonkovsky et al. (2007) | 1144 | ✓ | | | | S | S | S | S | S | S | S | | | | | |
| Thein et al. (2007) | 34 | ✓ | S | S | | S | S | S | S | S | S | S | | | | | |
| John-Baptiste et al. (2009) | 235 | ✓ | S | S | S | S | S | S | S | S | S | S | | S | | S | S |
| Sinakis et al. (2010) | 99 | ✓ | S | S | S | S | T | S | S | S | S | S | | | | | |
| Marcellin et al. (2011) | 1860 | ✓ | | | | S | S | S | S | S | S | S | | | | | |
| Bezeimer et al. (2012) | 128 | ✓ | S | S | | S | S | S | S | S | | | | | | | |
| Isaacs et al. (2013) | 118 | ✓ | | | | S | S | S | S | S | | | | | | | |
| Jerkehan et al. (2014) | 40 | ✓ | | | | S | S | S | S | S | | | | | | | |
| Younossi, Stepanova, Nader, et al. (2014) ^a | 192 | ✓ | | | | S | S | S | S | S | | | | | | | |
| Younossi, Stepanova, Henry, et al. (2014) ^a | 278 | ✓ | | | | S | S | S | S | S | | | | | | | |
| Younossi, Stepanova, Zeuzem et al. (2014) ^a | 215 | ✓ | | | | S | S | S | S | S | | | | | | | |
| | 201 | ✓ | S | T | S | S | S | S | | S | | | | | | | |
| | 327 | ✓ | | | | S | S | S | | | | | | | | | |
| | 334 | ✓ | | | | S | S | S | | | | | | | | | |

^a SVR12 reported.

2003). A lack of information and understanding of HCV at diagnosis could hinder this process however, denying the sought after sense of control and exacerbating prognostic uncertainty (Glacken et al., 2001; Sutton & Treloar, 2007).

The lived experience of HCV: fatigue

Fatigue is one of the most prevalent symptoms of HCV reported (Conrad, Garrett, Cooksley, Dunne, & MacDonald, 2006; Fry & Bates, 2012; Glacken, Coates, Kernohan, & Hegarty, 2003; Glacken et al., 2001; Groessl et al., 2008; Jiwani, Begum Gal, Ali, Salih, & Hanzala, 2013), and a greater understanding of how this impacts HRQoL starts to emerge when reviewing the qualitative data. The fatigue experienced has been described as discernible from 'normal fatigue' and multidimensional in nature, perniciously impacting on physical, cognitive and affective dimensions, creating a whole body feeling of fatigue which is unrelieved by rest (Glacken et al., 2003; Glacken et al., 2001):

"You cannot fight it; it is not a tiredness that you can fight like a normal tiredness. A normal tiredness, you can fight it and get a second wind or if you had a few cups of coffee, it would keep you going. None of this works with this tiredness" (Glacken et al., 2003, p. 247)

The unpredictability of symptoms has also proved challenging. A number of studies describe sporadic and episodic experiences of HCV illness (Conrad et al., 2006; Sutton & Treloar, 2007) which have a high impact on life when they occur, but when absent almost serve to reinforce a notion that the virus is not currently affecting health (Swan et al., 2010).

The lived experience of HCV: onward transmission

The possibility of passing the virus onto others has evoked strong reactions in a number of studies, with some participants citing it as a far greater HRQoL issue than any physical symptoms experienced (Conrad et al., 2006). Women have discussed worries over vertical transmission to children (Conrad et al., 2006; Temple-Smith et al., 2004), which in addition to causing possible disruption to plans for a family, can also impact sex lives and relationships (Grundy & Beeching, 2004; Jiwani et al., 2013; Lenton, Fraser, Moore, & Treloar, 2011). The knowledge that HCV is contagious, and subsequent fear of transmission to others, forms a large part of the psychological impact of living with HCV, eliciting constant feelings of anxiety and sadness (Hill et al., 2014).

The lived experience of HCV: impact on current IDUs

As previously mentioned, the reaction of current IDUs to an HCV diagnosis appears significantly less traumatic than those who stopped injecting many years ago and those who acquired HCV through another route. A lack of shock following the diagnosis (Faye & Irurita, 2003; Groessl et al., 2008; Harris, 2009) appears to be accompanied by a sense of inevitability linked to a high prevalence of HCV within their social networks (Hill et al., 2014; Olsen et al., 2012; Sutton & Treloar, 2007). A commonly reported consequence of HCV diagnosis is an intense and overwhelming depression, however in current IDUs this has been described as shallow, and nothing to be dwelt on (Faye & Irurita, 2003) epitomised by a "what's done is done, I can't change it now..." (Tompkins et al., 2005, p. 265) attitude. Davis and Rhodes (2004) note that HCV is constructed as something acquired rather than caught among the IDUs they interviewed in London, language that implies transmission is unavoidable, normalised and almost acquired over time; a ubiquitous risk. Wozniak, Prakash, Taylor, and Wild (2007) explored this apparent normalisation of HCV

amongst IDUs in Canada, describing HCV as a defining characteristic of injecting drug use. Further work from Australia reiterates these perceptions, with one study participant articulating her experience:

"And nobody talked about hep C really. I mean you know, in passing, it was just so assumed everybody had it. And nobody saw it as a big deal. No-one was thinking about it. Nobody thought it was anything other than just a complete minor detail that had no bearing on life at all" (Harris, 2009, p. 1032)

Roy, Nonn, Haley, and Cox (2007) suggest that an HCV diagnosis could actually have a positive significance for some, as it enables the individual to feel just like everyone else in their situation, or "...one of the gang, like" (Roy et al., 2007, p. 400). These ambivalent views towards disease diagnosis are at odds with Bury's (1982) account of biographical disruption, and instead appear to reinforce conceptions of self-identity and personal biography (Carricaburu & Pierret, 1995); HCV infection is synonymous with injecting drug use, and therefore injecting drug use will naturally lead to HCV infection (Olsen et al., 2012).

HCV may also have limited impact on life, as the diagnosis can be lost in a sea of multiple disruptions. In work with IDUs in Edinburgh, Copeland (2004) describes apathy towards having HCV perhaps stemming from multiple traumas faced in day-to-day life, and the significance of being HCV positive eclipsed by problematic existences and their identity as a 'problem drug user'. If the severity of HCV in relation to other more immediate life-threatening conditions (such as overdose) is considered, health problems that may not develop for many years such as those linked to HCV are unlikely to be overly concerning or prioritised, and activities that seek to improve an unimaginable future, such as HCV treatment, are not options worth investing in (Roy et al., 2007). Williams (2000) astutely notes that biographical disruption is perhaps more keenly felt among the privileged rather than disadvantaged sections of society.

As well as being contextualised within an individual's life, a diagnosis of HCV is often described in relation to HIV/AIDS (Copeland, 2004; Cullen, Kelly, Stanley, Langton, & Bury, 2005; Davis & Rhodes, 2004; Harris, 2009; Lekas, Siegel, & Leider, 2011; Munoz-Plaza, 2008; Roy et al., 2007; Swan et al., 2010; Tompkins et al., 2005; Wozniak et al., 2007). HIV is often defined as the primary viral risk for injecting drug use, with the seriousness of HCV being undermined by HIV (Davis & Rhodes, 2004). Excerpts from studies showing participants reactions at diagnosis serve to highlight this point:

"I wouldn't mind but I was in bits waiting for the results... the doctor was there going 'now... you have hepatitis C.' I was there going 'hurry up and tell me about the (HIV) virus'" (Cullen et al., 2005, p. 74)

"She told me 'everything looks fine, except it's written positive next to hepatitis C'. So I said to her, 'can I see? I hope I don't have AIDS'" (Roy et al., 2007, p. 400)

Even in HIV/HCV co-infection, a diagnosis of HCV can be over-shadowed by already having HIV (Copeland, 2004; Lekas et al., 2011). As public health harm-reduction messages for drug users historically centred on HIV prevention, HCV appeared within this framework later as an additional concern (Davis & Rhodes, 2004; Harris, 2009). This 'lesser of two evils' perception appears to pervade, with HCV presented as relatively benign in comparison to HIV, and cited as a reason why further investigations and treatment are not accessed post diagnosis (Swan et al., 2010).

The fact that HCV is often asymptomatic can also contribute to its low priority in lives with many competing demands. Although fatigue, cognitive impairment and depression are known symptoms, these are not ubiquitous, and where they do occur may not always be attributed to HCV, particularly where there is co-morbid active substance use. Due to the lack of physical impact there is no sense of threat from harbouring the virus (Fraenkel, McGraw, Wongcharatrawee, & Garcia-Tsao, 2005) and it therefore becomes an insignificant part of people's lives (Sutton & Treloar, 2007). Witnessing substance users 'living normally' and showing no signs of sickness can reinforce the normalisation and social accommodation of HCV within social networks, psychologically and socially preparing other members for a potential diagnosis (Carrier, LaPlante, & Bruneau, 2005; Faye & Irurita, 2003).

Reviewing these narratives as a whole, it could be easy to construe that all current substance users are disinterested in their health. However, despite repeated reports of an HCV diagnosis having little impact upon lives (Faye & Irurita, 2003; Olsen et al., 2012; Sutton & Treloar, 2007), there are examples of individuals reacting badly to the news (Sutton & Treloar, 2007; Tompkins et al., 2005). For some, an overwhelming sense of contamination has been described accompanied by a response characterised by despair (Fraser & Treloar, 2006). Rather than focusing the individual to address the cause however (by potentially seeking treatment), a number of accounts relate a sense that the infection is now with them for life, and as such interest in their health may actually decrease:

"Oh what's the use? You've got it, it's not going to go away, what's the use?" (Fraser & Treloar, 2006, p. 106)
 "What's the point? I'm either going to die from drugs or from liver disease" (Groessl et al., 2008, p. 1961). The authors note that immediately after diagnosis this participant began using drugs again.

The lived experience of HCV: stigma

The preponderance of accounts detailing individuals' experience of stigma in relation to HCV, create an overriding and pervasive theme within the literature on life experience, and again highlight its relative absence from the quantitative work. The stigma experienced is multifaceted, incorporating a number of factors including the involvement of an infectious agent (Conrad et al., 2006; Faye & Irurita, 2003; Fraser & Treloar, 2006) and an association with HIV/AIDS (Zickmund, Ho, Masuda, Ippolito, & Labrecque, 2003), however the most frequently described association is with illicit injecting drug use (Butt, Paterson, & McGuinness, 2008; Conrad et al., 2006; Faye & Irurita, 2003; Paterson, Butt, McGuinness, & Moffat, 2006; Zickmund et al., 2003). This link to substance use is persistent and tenacious, and stigma and discrimination related to substance use have been experienced by many individuals with HCV irrespective of their mode of acquisition (Butt et al., 2008; Faye & Irurita, 2003; Fry & Bates, 2012; Hill et al., 2014):

"We are all tarred with the same brush. People think 'hepatitis', yeah they're all drug addicts, and they think 'they've done something wrong'" (Hill et al., 2014, p. 5)

These stigmatising attitudes are encountered from family, friends, colleagues and also frequently within the healthcare setting (Butt et al., 2008; Fry & Bates, 2012; Grundy & Beeching, 2004; Hill et al., 2014; Janke et al., 2008; Jiwani et al., 2013; Miller et al., 2001; Sgorbini et al., 2009; Temple-Smith et al., 2004; Tompkins et al., 2005; Zickmund et al., 2003). Accounts from the literature also demonstrate an internalised stigma, whereby HCV positive individuals assimilate these widely held social views and

describe feeling contaminated, dirty or 'like a leper' (Fraser & Treloar, 2006; Glacken et al., 2001; Grundy & Beeching, 2004; Hill et al., 2014; Miller et al., 2001; Sutton & Treloar, 2007; Zickmund et al., 2003).

A decision not to disclose HCV positive status is often borne out of fears around subsequent stigmatisation (Butt et al., 2008; Conrad et al., 2006; Faye & Irurita, 2003; Fraser & Treloar, 2006; Glacken et al., 2001; Hill et al., 2014; Jiwani et al., 2013; Sgorbini et al., 2009; Sutton & Treloar, 2007; Tompkins et al., 2005), and can have a substantial impact on people's lives, for example by not identifying oneself as HCV positive, the opportunity to obtain support is lost (Faye & Irurita, 2003; Hill et al., 2014). In addition, any causal explanation for symptoms being experienced is removed, meaning individuals may have to continue working whilst extremely fatigued, or deny any emotional stress they may be suffering (Butt et al., 2008; Fry & Bates, 2012):

"It requires a constant vigilance on my part not to let it slip...you always have to appear 'normal' regardless of how you are really feeling" (Glacken et al., 2001, p. 110)

Non-disclosure can have more wide reaching implications. Butt et al. (2008) describe how one participant in their study quit his job and withdrew socially to conceal the diagnosis and associated symptoms. Although this voluntary social withdrawal may seem an extreme reaction, it serves to illustrate the impact of deep-seated and entrenched discrimination towards individuals with HCV which pervades unchanged throughout the historic literature up to the present day. Clearly, social isolation is not purely a voluntary undertaking however, and Glacken et al. (2001) describe the diagnosis of HCV resulting in participants feeling their 'social identity' had been stripped away, preventing them from maintaining previous social relationships.

The experience of HCV treatment

In addition to offering valuable insights into how HCV impacts on day-to-day life, the qualitative research also explores how the transient decrement in HRQoL reported in the quantitative literature is experienced, illustrating its impact on daily life and offering a greater depth of understanding. The side-effects of IFN-based therapy are expounded with a clear patient voice, illuminating their intense and persistent nature and contextualising their impact on the individual. These side-effects compromise employment opportunities and contribute to absenteeism (Hopwood & Treloar, 2005), affect physical appearance and changes in demeanour resulting in altered perceptions by others (Sheppard & Hubbert, 2006), and contribute to social isolation (Janke et al., 2008). The persistence of these symptoms throughout the course of treatment, and the unpredictability of onset are also significant factors contributing to the reduced HRQoL experienced (Fraenkel, McGraw, Wongcharatrawee, & Garcia-Tsao, 2006).

With insights into the lived experience of treatment and its side-effects, understandings into how these symptoms are managed and strategies for coping are also illuminated. Hopwood and Treloar (2008) focused on Resilience Theory, describing participants drawing on past experience of drug dependence, their history and experience of living with a chronic illness and challenges and lessons learned from a socially disadvantaged life. This theory is borne out in other studies, with examples of patients undergoing HCV treatment relating their use of anger management techniques learned at an alcohol treatment centre (Taylor-Young & Hildebrandt, 2009), and eschewing HCV support groups in favour of more familiar 12-step programmes previously attended (Sheppard & Hubbert, 2006). In addition to resilience, support

As with all syntheses of research, there are limitations to this review. There is the possibility that relevant literature has been inadvertently omitted, however the search strategies aimed to account for this through the use of multiple databases and broad search terms. Publication bias may be evident due to the inclusion of interventional studies in the quantitative arm, however discussion of the limitations of these has been made, and to exclude these from the review could itself lead to a narrative bias considering their abundance within the literature. To ensure all included articles were peer-reviewed, unpublished works were not included. Within the qualitative narrative, the included studies were conducted in different settings with a diverse group of participants, however the identification of broad key themes purposefully aimed to transcend these limitations and focus on shared insights. Finally, as previously mentioned, the variation in how drug use is reported within the published literature, and the lack of consensus on what constitutes 'substance use' or 'drug use', and poor definition of the terms 'active', 'current' or 'previous' drug use is problematic. For the purposes of this review, Supplementary files 1 and 2 make explicit the inclusion criteria stated in individual studies, however further clarity around this matter would benefit the interpretation of this literature as a whole.

Conclusion

Whilst the quantitative literature continues to report contemporary data on HRQoL with new treatment regimens (e.g. Younossi, Stepanova, Nader, et al., 2014), only one qualitative study reporting patient perspectives on HCV treatment since the advent of triple therapy has been published to date (Rasi et al., 2014), and as such a rounded contemporary understanding of HRQoL for individuals with HCV is absent. This review aims to catalyse further qualitative research in this area and to provoke discussion into the greater use of all HRQoL data within the development of clinical practice guidelines.

Conflict of interest

Within the three years preceding the start of work on this review, the lead author has received speaker fees from Janssen, and been on advisory boards and received travel and accommodation support to attend conferences and educational meetings from Janssen, MSD and BMS.

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Research paper

The lived experience of interferon-free treatments for hepatitis C: A thematic analysis



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ABSTRACT

Background: International discourse concerning the evolution in hepatitis C virus (HCV) therapy has tended to focus on improving outcomes, shortened treatment length and reduced side-effects of interferon-free regimens. How these treatments are being understood and experienced by the people receiving them has so far been overlooked. This study therefore aimed to explore the lived experience of individuals taking interferon-free HCV therapies.

Methods: Data were generated through 16 semi-structured interviews with a purposive sample of eight participants, recruited from a university hospital in Scotland. The interviews took place between June 2015 and March 2016, before and after a period of interferon-free HCV treatment. The data were interrogated using a thematic analysis, underpinned by social phenomenological theory.

Results: Three overriding themes were identified. 'Expectations and realisations' characterised the influence that interferon continued to cast over interferon-free treatment, contrasting the practicalities of taking interferon-free therapy with preconceived notions. 'An honour and a pleasure' portrayed a positive experience of an undemanding therapy, yet among those with a history of drug use, was also positioned as a privilege, associated with feelings of luck and guilt. 'Treatment needs' illustrated the strategies participants used to search for treatment efficacy, and the value those with a significant history of drug use placed on support. One nonconforming case is then discussed to enhance rigour and trustworthiness.

Conclusion: This is the first qualitative exploration of the experience of interferon-free HCV treatment reported globally. The results from this study suggest a cultural lag exists between the pharmacological developments which have been witnessed, and societal understandings of them. This has implications for the way services meet the needs of, and offer therapy to, HCV positive individuals.

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Background

Recent years have witnessed a rapid evolution in the treatment options available for people living with the hepatitis C virus (HCV) (Chung & Baumert, 2014; Pawlotsky et al., 2015). The summer of 2011 signalled the beginning of a new era in the fight against the disease, with the first direct-acting antivirals (DAAs) entering clinical practice in many high-income nations (Chung & Baumert,

2014). Although these drugs were initially added into the existing treatment regimen of pegylated interferon- α and ribavirin, swift pharmacological developments resulted in the advent of second generation DAAs which no longer required the notoriously unpleasant interferon- α backbone (Pawlotsky et al., 2015). These advances shortened the length of treatment to twelve weeks or less; reported a considerable reduction in side-effects; and improved sustained virological response (SVR) rates to over 90% (Asselah et al., 2016).

Globally, multiple barriers to accessing these medications at the patient-, provider- and governmental-level have led to only a minority of infected patients receiving them. Patient-level barriers include such issues as a lack of symptoms and social stigmatisation. Provider-level barriers encompass factors such as physicians'

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undue emphasis on purported contraindications to therapy (McGowan et al., 2013), such as exclusion criteria which penalise current injecting drug users. However, the barriers found at the governmental-level, largely concerning the high costs of these medications, are often cited as the most significant global barrier to patients receiving the best and most effective treatments available (Fung, 2015; Reau & Jensen, 2014). In Scotland, the high medication costs have led to restricted approval of a number of interferon-free regimens, allowing access for individuals with HCV genotype 1, but denying access to individuals with other HCV genotypes unless deemed ineligible for interferon-based therapy (Healthcare Improvement Scotland and NHS National Services Scotland, 2015). However, access to treatment is only one facet of achieving successful outcomes. Gaining insights into how HCV treatment is experienced and understood is also crucial when considering how treatments can be successfully delivered and monitored in clinical practice.

Qualitative investigation into the experience of taking interferon-based treatments has provided valuable insight into this arduous and demanding course of therapy for many years. The findings from this body of work have demonstrated the severity and persistence of a range of both physical and psychological side-effects, including chronic fatigue, flu-like symptoms, myalgia, insomnia, alopecia, weight loss, mood swings, anxiety, and depression (Fraenkel et al., 2006; Hopwood & Treloar, 2005; Kinder, 2009; Sheppard & Hubbert, 2006; Taylor-Young & Hildebrandt, 2009; Zickmund et al., 2006). Further, these studies have explored how this litany of treatment-related ailments has broader social implications. They describe how interferon-based therapy can affect an individual's self-identity and their perception by others (Janke et al., 2008; Sheppard & Hubbert, 2006), can strain relationships with family and friends (Sgorbini, O'Brien, & Jackson, 2009), and contribute to social isolation (Fraenkel et al., 2006; Janke et al., 2008; Taylor-Young & Hildebrandt, 2009). Accounts of interferon-based regimens are frequently framed as "horror stories" within the literature, emphasising the gruelling nature of treatment and the fear and anxiety it can produce (Kinder, 2009).

To date, there has been no similar exploration into the experience of taking interferon-free therapies. The prevailing discourse surrounding these new treatments emphasises their ease and tolerability (Coppola et al., 2015; Lam et al., 2015). However, this understanding is largely based on the results of quantitative health-related quality of life measures (Whiteley et al., 2015; Younossi et al., 2015a), which provide little context as to how an 'easier' treatment is actually experienced, and what it means for the individuals taking the medications. The aim of this study therefore, is to explore the lived experience of individuals taking interferon-free HCV therapies.

Methods

Theoretical framework

The study is underpinned by a social phenomenological framework. This sociological approach to phenomenology was first espoused by Schütz (1967), and emphasises the profound influence of the social world in establishing the meaning of a phenomenon. This approach to research rotates phenomenology outwards, exploring how the understanding of a phenomenon is founded in the inter-subjective social world, and challenges the eidetic phenomenological assumption that intentional consciousness is the driving force in constituting an object's meaning (Ajiboye, 2012). Social phenomenology seeks to explore the commonalities that are found in the subjective life-worlds of more than one actor, providing a more objective description and

understanding of a subjective experience (Shaw & Connelly, 2012).

Participants

This theoretical framework necessitated a qualitative study design, comprising in-depth, face-to-face, semi-structured interviews with eight participants, both before and after their period of treatment. Participants were purposefully sampled from an infectious diseases outpatient clinic based at a university hospital in Scotland. Inclusion criteria consisted of being aged 16 years or over, diagnosed with HCV for more than six months, and able to converse in English. A maximum variation sampling strategy was employed which aimed to select a heterogeneous sample of participants, who differed in their experience of previous HCV treatment, their mode of HCV acquisition and their date of diagnosis. This sampling strategy assumes that common patterns that emerge from great variation are of particular interest and value in capturing the shared dimensions of a phenomenon (Patton, 2015). Diversity within the sample also allows for the comparative potential of the data to be capitalised upon (Mason, 2002).

Individuals who fulfilled the inclusion criteria were approached by their regular HCV nurse or doctor during routine clinic appointments, and consent obtained for their details to be passed to the researcher (DW) if interest was shown in participating. Records were not kept of how many individuals were approached but declined to participate at this stage. Interested parties were then telephoned by the researcher, and a meeting arranged where the purpose of the study was explained, any questions answered, and written consent obtained to participate in one semi-structured pre-treatment interview, and to allow the researcher to contact them again with a view to conducting a further interview once their treatment was complete.

While all participants received interferon-free treatment, they did not all receive the same drug regimen. During the study, national guidelines and local recommendations for HCV treatment with DAAs were repeatedly revised, resulting in changes to first-line therapy. In addition, variations in regimen occurred in line with factors such as degree of liver disease and HCV genotype. Also, one participant undertook an unlicensed interferon-free regimen as part of a separate randomised controlled trial. These factors resulted in the use of four different treatment regimens among the eight participants (Table 1). In order to protect participant anonymity, the details of which regimen each individual received have not been specified. However, whether these regimens were single- or multi-tablet has been noted alongside participant quotes within the results.

Interviews

All interviews were conducted between June 2015 and March 2016 within a suitable room at the hospital outpatient clinic, and lasted a mean duration of 40 min. Topic guides were used, however the semi-structured approach allowed participants the freedom to talk about their personal experiences as they wished. The pre-treatment interviews covered HCV treatment knowledge and perceptions, previous experiences of HCV therapy, and thoughts and feelings about their proposed course of medication. The questions posed to the participants were designed to be brief, simple and open-ended (e.g. "can you tell me what you know about hep C treatment?") with their answers probed for further detail where appropriate. Follow-up interviews focused on the participants' experiences of treatment and their views on the treatment service. In addition, during the post-treatment interviews, transcript excerpts from the participant's pre-treatment interview

Table 1
Details of the four different HCV treatment regimens taken by participants.

| Treatment regimen | Single- or multi-tablet regimen | Number of participants |
|--|---------------------------------|------------------------|
| Sofosbuvir/ledipasvir (<i>Harvoni</i> [®]): combination tablet taken once daily. Licensed for use within Scotland for the treatment of HCV genotype 1 and 4, and for restricted use in genotype 3 (Scottish Medicines Consortium [SMC], 2015a). | Single-tablet | 4 |
| Ombitasvir/paritaprevir/ritonavir (<i>Viekirax</i> [®]) + dasabuvir (<i>Exviera</i> [®]) + ribavirin: a combination tablet taken once daily, in conjunction with two twice daily medications. Licensed within Scotland for the treatment of HCV genotype 1 (SMC, 2015b). | Multi-tablet | 2 |
| Sofosbuvir (<i>Sovaldi</i> [®]) + daclatasvir (<i>Daklinza</i> [®]) + ribavirin: combination of two once daily tablets in conjunction with one twice daily medication. Licensed in Scotland for use in the treatment of patients with significant fibrosis or compensated cirrhosis in genotypes 1, 3 and 4 (SMC, 2014). | Multi-tablet | 1 |
| Glecaprevir + pibrentasvir: fixed dose combination with pangenotypic action, currently in phase III clinical trials. Not currently licensed for use in Scotland (UK Medicines Information, 2016) | Single-tablet | 1 |

were used to revisit their specific expectations and thoughts about treatment from a different standpoint. All interviews were conducted by DW, a registered nurse with ten years' experience and who had worked as an HCV nurse specialist between 2009 and 2013. No access to paper or electronic patient case notes was permitted during the study. The interviews were recorded using an encrypted digital audio-recorder, and field notes were made upon completion and added to a research diary. Audio-files of the interviews were transcribed verbatim by DW, during which any patient identifiable information was obscured from the narrative.

Analysis

Six phases of thematic analysis guided the analytical process (Braun & Clarke, 2006). Each transcript was initially read and reread in full by two researchers (DW and AW) in order to ensure subsequent coding and identification of themes remained firmly rooted in the narratives. Coding was then conducted by DW using NVivo v.10 software, and contained both deductive and inductive elements. A broad coding framework was initially devised, informed by categories found in previous qualitative research focused on interferon-based therapy, such as 'side-effects' and 'support' (Whiteley et al., 2015). It was considered reasonable to assume that wide-ranging categories such as these may be a feature of any treatment experience, transcending the specifics of the medications involved. More detailed inductive codes were then added to this basic structure, formed from initial impressions of the corpus of data following further readings of the transcripts. This approach served to assist with the early analysis of the data, however codes were also developed as novel and unexpected insights were met. The pre- and post-treatment interviews were compared and contrasted, with both sets of data contributing to the generation of codes. As analysis progressed, the deductive categories were dismissed, and the inductive codes combined, reviewed and revised. This process drew groups of codes together to form a number of sub-themes. While depicted as a linear progression, the interviewing, transcribing and coding process occurred in parallel, with each activity informing the others. This iterative process aided the identification of data saturation; no new codes were created during the coding of the final two transcripts as the narratives aligned with sub-themes already developed. The sub-themes were then combined into candidate themes which were examined in relation to the corpus of data, field notes, and the research diary. During this process, all four authors met regularly to review, challenge and interrogate the evolving analysis.

The trustworthiness and rigour of this endeavour were enhanced in a number of ways. Regular meetings between all authors helped to contest and question any preconceptions or assumptions DW may have brought to the study due to his work history, consistent with the concept of bracketing. Within social phenomenological research, the focus of study is the inter-subjective consciousness of which we, as researchers, are a part.

In order to study this inter-subjective consciousness, the concept of bracketing demands that we suspend belief in the existence of the world as we know it, and allow doubt that the world could be anything other than it appears (Ritzer & Ryan, 2011; Schütz, 1967). Meeting the participants on more than one occasion allowed initial interpretations to be revisited and verified, and ideas expressed pre-treatment to be reconsidered by both the participant and the interviewer. Immersion in the full dataset by two of the authors ensured the findings remained data-driven and rooted in the narratives, rather than becoming too removed from the participants' voice. Where available, nonconforming cases were included in the analysis, to take into account an alternative and legitimate perspective on treatment.

Ethical approval

The study was reviewed and approved by the South East Scotland NHS Research Ethics Committee 01 (15/SS/0010) and by Edinburgh Napier University Research Ethics Committee. All participants were offered a £15 supermarket gift voucher for each interview they completed in line with national guidelines.

Results

The characteristics of the sample are shown in Table 2. Each individual participated in two interviews, pre- and post-treatment, with no participant drop out during the study. The themes which

Table 2
Demographic information for the eight participants. All information was self-reported by the participants during their initial interviews.

| | | |
|--|--------------------|---|
| Gender | Male | 6 |
| | Female | 2 |
| Ethnicity | UK | 6 |
| | Other | 2 |
| Age | 0–39 | 1 |
| | 40–49 | 2 |
| | 50–59 | 5 |
| Opioid substitution therapy? | Yes | 3 |
| | No | 5 |
| Mode of acquisition | Injecting drug use | 5 |
| | Other | 3 |
| Date of diagnosis | Up to 2011 | 4 |
| | 2011 and after | 4 |
| Degree of liver disease | Pre-cirrhotic | 6 |
| | Cirrhotic | 2 |
| Previous interferon-based HCV treatment? | Yes | 2 |
| | No | 6 |

resulted from the analysis: expectations and realisations; an honour and a pleasure; and treatment needs, will now be examined.

Theme: expectations and realisations

The participants' initial impressions of HCV treatment were unvaryingly negative, and bound to the interferon era. They recounted a demanding and arduous course of therapy, gathered from various 'horror stories', or through witnessing others taking interferon-based treatment first-hand:

I talked to people an' all, all I got to hear was – this interferon is killing me, this interferon is killing me, I don't know if I can keep on doing this. (Gary, multi-tablet regimen)

Despite each participant receiving an interferon-free regimen, and being prepared and counselled for such by their healthcare team, the discourse surrounding treatment expectations was entangled with societal understandings of interferon-based therapy. The influence of the drug that defined and characterised HCV treatment for over 20 years was prominent within the narratives. 'Normal' life would be forfeit for the duration of their interferon-free therapy, and the potential cure would come at a short-term cost:

... I mean, if I spent three months of feeling a bit groggy, tired and miserable and I come out in the end, with err, you know, with err, good err, blood, err then it's, you know, it's worth that sacrifice ... (John, multi-tablet regimen)

Common side-effects of interferon were referenced explicitly as expectations for interferon-free treatments, with discussion of practical preparations to forestall the impact of these perceived inevitabilities commonplace. For Stewart, the strength of his beliefs around the detrimental effect of treatment on his wellbeing was demonstrated in the meticulous planning that accompanied his first dose of the drugs:

First tablet, went home, sick bowl, towel, duvet, tissues, waiting for it to come on (...) I prepared ready to be sick, I'd, I'd sent my partner away in case I was, really ill, know, kind a', I don't want a' be sick or, or screaming at people. I thought I was gonna be agitated, angry ... (Stewart, single-tablet regimen)

Interferon was styled as a powerful and toxic drug within the narratives, and this perception of pharmacological strength was maintained when discussion turned towards DAAs. The perceived strength of these drugs equated with the expectation of physiological collateral damage. The idea of 'no pain no gain' prevailed. An unpleasant, demanding and strenuous period of treatment must surely result from drugs formidable enough to eradicate HCV.

For the majority of participants, the realisation of their worst fears and expectations did not materialise during their period of therapy, however a discourse surrounding treatment side-effects did become evident. Examination of these narratives revealed a generally mild and manageable experience, significantly removed from the imagined horrors of therapy which had been so vividly constructed. Side-effects were rarely stressed or emphasised, more commonly mentioned in passing or casually alluded to as minor inconveniences. Descriptions of specific physical ailments were embedded within concurrent narratives of feeling well, and having little to complain about:

... because physically I was fine, I cannae say there was anything really bad, the first two weeks, the headaches an' I got quite a lot a' bleeding noses, but then I jus' started sort a' taking painkillers for the headaches, then ... when I came [to the clinic], I had quite a bit a' constipation, so they gave me

something for that, but that was it, nothing else. (Danielle, single-tablet regimen)

In addition to physical side-effects, a number of participants also related accounts of low mood and transient depression during treatment, however potential explanations for these ailments encompassed more than the pharmacology of the drugs. The physical act of taking HCV therapy brought the disease to the forefront of participants' minds, and meant confronting a reality many had previously been able to put to one side:

... it's got a lot to do wi' the mental side of it like, y'know, because you're really wanting this treatment a' work an you're conscious of it, you're conscious of always being on this treatment, so likes, when I wasn't I, I'd forget about it for months, I forgot all about I had hep C. Y'know what I mean? (Steve, multi-tablet regimen)

Emotional strain during the treatment process grew from the importance participants placed on being cured of HCV. However, the impact on mental health from interferon-free treatment was considered and framed in respect to the imagined greater influence that interferon-based therapy would have, and as such its significance was diminished and symptoms became manageable. For example, the account above appeared towards the end of Steve's narrative, almost as an afterthought or addendum. Earlier in his interview Steve had described his treatment as "nowhere near as bad on your mental health as [interferon]" and how he "thought the medication was fantastic".

Despite an impression of the side-effects of interferon-free therapy being comparatively innocuous, every participant drew attention to other difficulties which they had encountered during treatment. The physical size of the tablets and the difficulty in swallowing them were emphasised, and for those on multi-tablet regimens, a sense of being misled as to the simplicity of treatment became noticeable:

The, the biggest thing that I think, was the fact when the new treatment came out it was, it sounded more like it was jus' like more or less a single or two single type a' tablets (...) even though the course was of three, four, five – ten different tablets that I was taking during the day anyway, so, that was the only thing that I was slightly sceptical in the way that that came across ... (Gary, multi-tablet regimen)

The accounts of participants on multi-tablet regimens underscored how the therapy was not taken in isolation, but incorporated into a life which was often already crowded with complex polypharmacy. Opioid substitution therapy, anxiolytics, anti-psychotics and anti-retrovirals were just some of the medications participants reported as part of their daily routine. Pill burden remained a significant feature of their course of treatment.

Theme: an honour and a pleasure

The majority of participants related a largely positive and favourable account of their treatment, constructing their experience of interferon-free therapy as physically undemanding and relatively straightforward. The short length of treatment and reduction in side-effects in relation to socially informed understandings of interferon-based therapy were framed as the most significant benefits of interferon-free regimens. Participants who had previous first-hand encounters of interferon-based treatment were able to make contrasts with those eventful and side-effect laden experiences:

... it was all easy, compared to the last time, 'cause I ... 'cause I done the treatment, the interferon one, an' compared to that,

this was a breeze [laughs], this was like, jus' like taking y'know, Lemsip or something ... (Keith, single-tablet regimen)

While the participants' narratives were largely positive in tone, a perception from some that they had been fortunate or lucky to access these treatments underpinned the discourse. Those with histories of drug use described feeling guilty at what they perceived as good fortune of being in the right place at the right time, underlining an understanding that interferon-free therapy was not available to everyone, but a privilege and an honour. For John, the guilt he experienced was rooted in his perception that some degree of atonement should be necessary to cure a disease which he felt he had brought upon himself. The ease and simplicity of his treatment experience jarred with his belief that a penance should be paid for the removal of HCV from his life, and that he had got away lightly compared to others he knew. John felt he had escaped HCV with impunity, and this unsettled him:

I'll tell you why I felt guilty about it – I've got a really close friend who's got like this medical situation, an' he copes with it brilliantly, an' he, erm, he hadn't caused it himself or anything, he was jus', y'know, erm, suffering from this condition an' he has to struggle along an' get on with it, y'know, an' I've jus' been more or less given a solution to my problem an' have kind of got away with it scot-free. (John, multi-tablet regimen)

In addition to feeling fortunate in comparison to other people, participants' awareness of the cost of the drugs contributed to their sense of honour in receiving these therapies. While feelings of shock at the expense of the medications were voiced, these views contributed to a sense of privilege in gaining access to medications which were not universally available. The price-tags of these medications were not only discussed in relation to other treatments for HCV, but also in the context of distributive justice within other diseases:

It makes me feel ... bloody privileged, 'cause, y'know what I mean, 'cause ... no' many people are getting that, I mean there's people out there that've got cancers an' stuff an' they're getting knocked back for treatments that cost that much. (Keith, single-tablet regimen)

A few participants mentioned the media as the source of their information on medication costs. However, a number of others implied that this knowledge was explicit in the discourse of the treating healthcare team, with participants trained in the price of their cure from an early stage:

I knew that fae, the first week, how much these, all these cost an' all that, I mean coming here you get taught, you get told what they're trying a' do here, an' you find out how expensive they all are ... (Stewart, single-tablet regimen)

The narratives of some participants suggested the guilt and privilege felt at being able to access such expensive therapies had implications which extended beyond HCV therapy. The experience of being prescribed these drugs strengthened, or built a resolve, that the investment made in them, both financially and personally, would reap long-term rewards:

I feel sort a', it makes me, it'll make me think twice about going back taking drugs or alcohol or getting, going back on that kind a' thing when you, you've been privileged enough for people a' fight to get you better. (Keith, single-tablet regimen)

Theme: treatment needs

The belief that HCV treatment should be an onerous undertaking, rather than a straightforward and undemanding process, constructed a compelling discourse relating how participants subsequently searched for signs and indicators that their treatment was working. A need to substantiate the efficacy of

the drugs permeated the participants' narratives, shaping a perception that side-effects were almost desirable and advantageous:

... when I came after four week I ask [the HCV nurse], she said do you feel anything? Are you tired or this? An' I say no, I say actually sometime I think I'm on a placebo, because there is no any effect at all. (Peter, single-tablet regimen)

The hunt for side-effects increased the likelihood that any irregularities may be attributed to treatment, and relatively minor events such as single bouts of diarrhoea, or episodes of absent-mindedness were automatically ascribed to the medications. The identification of possible side-effects was not the only method by which markers of efficacy were sought however. The importance to participants of hearing how they were progressing through treatment from healthcare professionals also became a recurring refrain within the narratives. The significance of receiving results from routine blood tests detailing the downward trajectory of the HCV viral load was repeatedly emphasised, situating them as beacons of reassurance, hope and motivation:

... I started off really high, I was [x] million, which is very very high, an' I went down to [states much lower figure] within three weeks – that's impossible! Err, so, it's when you find out how quickly the treatment is working, err, in the first three week period an' you're thinking – that's only three weeks, so it gives you that massive hope, y'know ... (Steve, multi-tablet regimen)

In addition, a couple of participants described a further instinctive approach to evaluating the effectiveness of treatment; they simply felt better while taking it. Primarily describing a feeling of reduced fatigue, this discourse was present in the narratives of those participants taking interferon- and ribavirin-free regimens:

... maybe the hepatitis made me slow down but I didn't realise, an' I thought it was jus' age! An' then I thought, I supposed to be feeling less energetic [on treatment], but, I want to do things all the time (...), it was fantastic, because I was feeling better after the four weeks, I say I feel more energy ... (Peter, single-tablet regimen)

Support was framed in broad terms within the discourse, not solely focused on the practicalities of HCV treatment, but viewed more holistically, as caring for the complete individual. While support was acknowledged by all participants, a sharp contrast became evident in the perceived value and need for that support between participants who recounted extensive and graphic histories of drug use, and those who did not. For those who did not, the support received, although highly regarded, was ultimately deemed unnecessary on retrospective reflection:

No, no, not at all, no, no. No. Not with [this drug], nothing at all, I never felt I needed any support with [this drug], not at all, not at all. (Happy, single-tablet regimen)

By contrast, the discourse from those with a history of drug use and drug dependence treatment emphasised the significance of support, highlighting its value to both practical and emotional aspects of therapy:

... it is quite hard to jus' keep it, doing it yourself (...) it's really quite difficult, erm, you may think oh it's easy jus' take it err next, nine in the morning, nine at night, but likes, when you're not working an' you're likes, err, like I said, really heavily medicated, it doesn't work out like that ... (Steve, multi-tablet regimen)

Interviewer: Was [the support received from the HCV treatment centre] important to you?

Keith: Aye, it was good to come here.

Interviewer: Why?

Keith: The mental, the friendship, the feeling a' care, people caring about you, d'you get what I mean? If you do that in the community you're jus' going in a' see somebody, you're getting your tablets an' you're fucking off for three months, it's no' gonna be the same. You're no' gonna have that ... (Keith, single-tablet regimen)

For these individuals, support was portrayed as an expected, integral and essential component of the HCV treatment package, irrespective of the HCV drug combination or ease of therapy. This is well illustrated by Danielle, who felt short-changed and cheated by her interferon-free course of therapy compared to other people she knew prescribed interferon-based regimens:

... oh, I don't know how a' explain this one really. I think people are all getting treated differently, right, when you're on triple therapy, right, you're getting all the support, all the support, money-wise, mentally, the doctors, all the rest a' it, this therapy you dunnae get nothing. (Danielle, single-tablet regimen)

Of note, peer support was repeatedly mentioned as being of particular worth to this sub-group of participants. They spoke of the immense value it had contributed to their experience, and positioned repaying that support, and using their own experience to benefit others, as a natural and obvious next step. For Gary, this step had already been taken as he described placing himself at the centre of a local support network:

... speaking out aloud at the group an' being one of the fore [pauses] I was gonna say forefathers there! Because we've jus' kinda taken it from nowhere an' we've put ourselves up for being this support, support group, now we're looking at the angles where we can, can take things ... (Gary, multi-tablet regimen)

A nonconforming account

Gary's experience of treatment grated with the predominant discourse emerging from the other participants. While the expectation of a demanding course of therapy was widely held, Gary was alone in having his worst expectations confirmed:

... I started getting quite violently ill, sick, migraines, constant headaches were coming along, I spent about two weeks, literally, feeling like vomiting, couldn't move off the sofa, lying in the same clothes, never had any energy, very lackadaisical, very very aggravated, I got myself so agitated, they ended up putting me on erm ... [an antipsychotic], 'cause a' my, I was so, getting so stressed ... (Gary, multi-tablet regimen)

While Gary was not alone in experiencing side-effects, his account was unusual in the prominence he gave them. He characterised his experience of treatment as one of illness and disorder, in contrast to other participants whose narratives mainly emphasised wellness and vitality punctuated by occasional complaints. It is possible that these medications may have severe adverse side-effects for a minority of people taking them. However, Gary's narrative displayed a depth and intensity of expectation which was noticeable among the collected testimonies, and positioned his temporary illness as an absolute necessity in order for his therapy to be effective:

... I, I, I kinda got to that stage where I knew, for treatment to be successful, there's gonna be, there's gonna be elements a' illness in there, it's gonna do things to your body, so – aye, I kinda jus' kept my mind in that ... (Gary, multi-tablet regimen)

... jus' because I knew, listen, this is part of it, an' I kinda structured my mind so I know I've gotta get ill to get better type a' thing. (Gary, multi-tablet regimen)

While initially appearing divergent from the prevailing discourse, Gary's narrative strengthens and augments many key aspects of the themes found within the collected data, emphasising the importance of considering the themes collectively, rather than in isolation. Although he did not describe the primarily positive experience of treatment constructed by the other participants, he acknowledged the luck he felt in receiving it, and assembled an account which reinforced the discourse concerning treatment needs and the hunt for efficacy. While it is possible that Gary experienced an atypical physiological reaction to the medication he was given, the side-effects he experienced may also have been borne of a belief that HCV therapy needed to be powerful, and the more toxicity he experienced, the greater the chance of the treatment working. His testimony suggests that despite his difficulties, he believed the treatment he was taking was having a curative effect:

I never ever thought to myself I'm gonna stop this treatment, but there was, that niggling in the back of my head saying – can you carry on? I thought, no, I've come this far, I'm, I'm not gonna back out an' stop my treatment, no matter how hard-core it is ... (Gary, multi-tablet regimen)

Discussion

Quantitative reports of health-related quality of life during interferon-free HCV treatments have noted improvements in both mental and physical health domains compared to interferon-based regimens (Younossi et al., 2015a, 2015b, 2015c). To date however, qualitative interpretations of the lived experience of these treatments have remained absent, preventing any contextual insights into the meaning of these numeric reports of 'easier' therapies.

The experience of interferon-free HCV treatment is illustrated by the three themes previously described. These themes do not exist in isolation, but interweave within and between each individual narrative, demonstrating how understandings which have been presented discretely, are necessarily intertwined. For example, the self-monitoring and importance of support described within 'treatment needs' was not only the product of participants questioning an easier than expected treatment, but was also integral to the construction of that positive experience. That is not to say tensions do not exist. For example, the accounts of side-effects discussed in 'expectations and realisations' sit uneasily next to the discourse which described participants hunting for non-existent side-effects in 'treatment needs'. These two positions should be considered in counterpoise to one another, where equilibrium was maintained between the volume and intensity of side-effects experienced and the proactive search for further signs of efficacy. This illustrates the way in which apparently contradictory aspects of these themes wax and wane in relation to each other, emphasising their fundamental interdependence.

This study reveals the legacy of interferon- α currently casts a long shadow over the experience of interferon-free regimens, with the participant testimonies intricately tied to the historical touchstone of interferon-based treatment. For example, discussion of side-effects continued to dominate the narratives. However, while the burden and severity of these ailments was the historical focus of concern (Hopwood & Treloar, 2005; Kinder, 2009; Sheppard & Hubbert, 2006), it was disbelief at the relative absence of side-effects which now took precedence within the participants' accounts.

The understanding of HCV therapy as a rigorous and demanding undertaking, informed the notion that effective treatment must be

accompanied by toxicity and short-term suffering. Insights gained from this study suggest participants actively sought out side-effects from interferon-free therapies as biomarkers for the effectiveness of the drugs, echoing reports from the interferon era which found participants expecting to be unwell in order to get better (Taylor-Young & Hildebrandt, 2009). Although not widely reported, this phenomenon has been noted in other disciplines, particularly in the fields of oncology and rheumatology (Goodacre & Goodacre, 2004; Gradishar, 2015; Lorish, Richards and Brown, 1990), with periodic reports of patients requesting more aggressive and noxious therapies in the belief that these equate with improved efficacy (Gradishar, 2015; Trusson & Pilnick, 2016). This insight exposes a cultural lag between the rapid pharmacological developments which have been witnessed, and the social understanding of them, creating conflict between what patients *ought* to need, and what they actually require.

While the majority of participants recounted a relatively straightforward period of therapy (the exception being Gary), the discourse of luck and guilt was solely located in the narratives of those participants with histories of drug use. This resonates with the acceptance of health inequalities, lack of entitlement, and the tolerance of rights violations which disenfranchised HCV communities have grown accustomed to over the years (Wolfe et al., 2015). The discourse of luck and guilt positions those participants with histories of drug use as submissive recipients of healthcare, rather than active and emboldened consumers. The absence of this narrative from the three participants who did not identify as drug users only serves to illustrate this point more effectively. However, the 'privilege' of treatment may also promote wider beneficial outcomes. Transformation narratives within the data suggest undertaking a course of interferon-free therapy may positively affect an individual's self-worth, and aid personal rehabilitation, consistent with previous studies conducted during the interferon era (Batchelder et al., 2015; Clark & Gifford, 2014; Rance et al., 2014).

All participants in this study successfully completed their treatment regimen, and subsequently achieved an SVR. Their treatment was delivered through a hospital-based clinic, however there is an emerging evidence base that moving therapy away from secondary care and into more diverse settings is a feasible objective (Alavi et al., 2013; Brew, Butt & Wright, 2013). Interferon-based treatments have been successfully delivered in opioid substitution settings and prisons, achieving comparable adherence and response rates to those reported in more conventional locations (Grebely et al., 2016; Litwin et al., 2009; Rice et al., 2012), but these support-intensive models of treatment delivery may be reviewed in light of fewer perceived patient requirements with 'easier' drugs. As interferon-free (and increasingly ribavirin-free) treatments proliferate, the clinical need for close haematological and side-effect monitoring of patients recedes (Lam et al., 2015), however the significance of knowing the treatment to be working, and the continued importance of support for individuals with significant histories of drug use and drug treatment are key findings within this analysis. While the global HCV discourse tends to focus on improving SVR rates, reduced side-effect profiles and decreasing treatment times (Asselah et al., 2016; Chung & Baumert, 2014; Pawlotsky et al., 2015), understanding what motivates and reassures individuals while taking the drugs is essential in ensuring improved adherence and integral to interferon-free treatments reaching their full potential. The cultural lag observed within this study suggests caution should be exercised in any reconsideration of how best to deliver interferon-free therapies to patients, as the experience of interferon-free treatment continues to demonstrate a significant and essential discourse of needs.

How these needs are met is an important consideration. The value placed on peer support was evident within the narratives, and

emphasises that participants' appreciated support which came from within their own communities and social networks. Peer support has been recognised as an important factor in the facilitation of access to HCV services for populations that may experience significant barriers to accessing care (Crawford & Bath, 2013). The ETHOS project in Australia has repeatedly demonstrated how peer support workers within opioid substitution clinics perform a valuable role in reducing barriers to HCV care and treatment, and how these workers are regarded as highly credible and trustworthy by those they support (Keats et al., 2015; Treloar et al., 2015). Peer support has been cited as one of ten priorities for expanding access to HCV treatment among drug users in low- and middle-income countries (Ford et al., 2015), and this study suggests its value also extends to other more traditional care settings in high-income nations.

The differing account provided by Gary also highlights an important consideration; these themes and findings must be considered within the context of each individual person. The nocebo phenomenon, in which placebos produce adverse side-effects, can also offer insight into the reporting of nonspecific side-effects in patients taking active medications (Faasse & Petrie, 2013). Patient expectations and pre-treatment conditioning are often designated as key constituents of this phenomenon. However, there are numerous personal, psychological, situational and contextual factors which have also been identified as potential components, such as learning from past experiences, and pre-existing anxiety and depression (Barsky et al., 2002). While the thrust of this analysis stems from a realisation of largely unmet pre-treatment expectations, there may be particular individuals whose specific set of circumstances and attributes allows those expectations to be realised. Gary's narrative accentuates the importance of a contextual understanding of interferon-free treatment.

This study has a number of limitations. The participants were all recruited from a hospital-based outpatient clinic, and may therefore be more engaged with healthcare and knowledgeable about HCV treatment. The sample was also drawn from one treatment site within one geographical area, however the findings are transferable to other localities which have similar methods of treatment delivery and serve similar populations of individuals with HCV. The sample size was also small, and the findings are therefore exploratory in nature. Finally, while the participants were prescribed different interferon-free therapies, the primary focus of analysis was not the variation between interferon-free regimens, but how HCV treatment is understood and experienced when it no longer includes the one drug, interferon- α , which has defined and characterised it for over 20 years.

Conclusion

This is the first qualitative exploration of interferon-free HCV treatment reported globally. It reveals that the perception of interferon-free treatment remains entwined with cultural understandings of interferon-based therapies. Despite an acknowledgement that interferon-free treatment was less physically and emotionally demanding than expected, the importance of support and reassurance remained integral to the experience of therapy for those individuals with a significant history of drug use. The way in which these medications are delivered in clinical practice now, and in the immediate future, should acknowledge and take these findings into account.

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Conflict of interest

Within the three years preceding the start of this work, the lead author served as a speaker for Janssen.

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Appendix B

Literature search strategies

Table 6: Initial search strategy for quantitative articles detailing the HRQoL for individuals with HCV within each individual database, and the results achieved. Searches last run 17 November 2016.

| Search Engine | Search Terms (ST)/Subject Index Terms (SIT) | # Retrieved | # Remaining following title/abstract exclusions & duplication exclusions |
|------------------------|--|-------------|--|
| Medline | S1: Hepatitis C (SIT) OR Hepatitis C, Chronic (SIT) OR Hepatitis C (ST) | 76,577 | |
| Medline | S2: Patient Outcome Assessment (SIT) OR Patient Reported Outcomes (ST) | 7,336 | |
| Medline | S3: Quality of life (SIT) OR Health Related Quality of Life (ST) | 77,738 | |
| Medline | S4: HRQL (ST) | 2,843 | |
| Medline | S5: HR-QOL (ST) | 554 | |
| Medline | S6: HRQOL (ST) | 10,716 | |
| Medline | S7: S2 OR S3 OR S4 OR S5 OR S6 | 83,758 | |
| Medline | S8: S1 AND S7 | 402 | 143 |
| Database Total: | | | 143 |
| CINAHL | S1: Hepatitis C (SIT) OR Hepatitis C, Chronic (SIT) OR Hepatitis C (ST) | 12,054 | |
| CINAHL | S2: Outcome Assessment (SIT) OR Outcomes [Health Care] (SIT) OR Patient Reported Outcomes (ST) | 59,271 | |
| CINAHL | S3: Quality of life (SIT) OR Health Related Quality of Life (ST) | 40,279 | |
| CINAHL | S4: HRQL (ST) | 783 | |
| CINAHL | S5: HR-QOL (ST) | 128 | |
| CINAHL | S6: HRQOL (ST) | 3,170 | |
| CINAHL | S7: S2 OR S3 OR S4 OR S5 OR S6 | 97,662 | |
| CINAHL | S8: S1 AND S7 | 279 | 10 |
| Database Total: | | | 10 |
| Embase | S1: Hepatitis C (SIT) OR Hepatitis C Virus (SIT) OR Hepatitis C (ST) | 122,750 | |
| Embase | S2: Outcome Assessment (SIT) OR Outcomes Research (SIT) OR Patient Reported Outcomes (ST) | 36,864 | |
| Embase | S3: Quality of Life (SIT) OR Health-Related Quality of Life (ST) | 113,752 | |
| Embase | S4: HRQL (ST) | 4502 | |
| Embase | S5: HR-QOL (ST) | 876 | |
| Embase | S6: HRQOL (ST) | 17,155 | |
| Embase | S7: S2 OR S3 OR S4 OR S5 OR S6 | 147,265 | |
| Embase | S8: S1 AND S7 | 887 | 25 |
| Database Total: | | | 25 |
| Cochrane Library | S1: Hepatitis C (ST) | 702 | |
| Cochrane Library | S2: Quality of Life (ST) | 5128 | |
| Cochrane Library | S3: S1 AND S2 | 486 | 0 |
| Database Total: | | | 0 |
| JBICoNECT+ | S1: Hepatitis C (ST) | 12 | 0 |
| Database Total: | | | 0 |
| PsycINFO | S1: Hepatitis (SIT) OR Toxic Hepatitis (SIT) OR Hepatitis C (ST) | 3,031 | |
| PsycINFO | S2: Quality of Life (SIT) OR Quality of Life (ST) | 69,363 | |
| PsycINFO | S3: S1 AND S2 | 185 | 5 |
| Database Total: | | | 5 |
| ASSIA | S1: Hepatitis C (ST) | 1,117 | |
| ASSIA | S2: Quality of Life (SIT) OR Health Related Quality of Life (ST) | 14,852 | |
| ASSIA | S3: S1 AND S2 | 32 | 0 |
| Database Total: | | | 0 |

Table 7: Initial search strategy for qualitative articles detailing the lived experience of HCV used within each individual database, and results achieved. Searches last run 18 November 2016.

| Search Engine | Search Terms (ST)/Subject Index Terms (SIT) | # Retrieved | # Remaining following title/abstract exclusions & duplicate exclusions |
|------------------------|--|-------------|--|
| Medline | S1: Hepatitis C (SIT) OR Hepatitis C, Chronic (SIT) OR Hepatitis C (ST) | 76,588 | |
| Medline | S2: Quality of life (SIT) OR Quality of life (ST) OR Life Changes Events (SIT) OR Experience (ST) | 756,245 | |
| Medline | S3: S1 AND S2 | 2,748 | |
| Medline | S4: Qualitative Research (SIT) OR Qualitative (ST) OR Interviews as Topic (SIT) OR Interview, Psychological (SIT) OR Interview* | 408,096 | |
| Medline | S5: S3 AND S4 | 166 | 46 |
| Database Total: | | | 46 |
| CINAHL | S1: Hepatitis C (SIT) OR Hepatitis C, Chronic (SIT) OR Hepatitis C (ST) | 12,054 | |
| CINAHL | S2: Quality of Life (SIT) OR Quality of Life (ST) OR Life Experiences (SIT) OR Experience (ST) | 240,348 | |
| CINAHL | S3: S1 AND S2 | 540 | |
| CINAHL | S4: Qualitative Studies (SIT) OR Qualitative (ST) OR Interviews (SIT) OR Interview* (ST) | 251,558 | |
| CINAHL | S5: S3 AND S4 | 104 | 14 |
| Database Total: | | | 14 |
| Embase | S1:Hepatitis C (SIT) OR Hepatitis C Virus (SIT) OR Hepatitis C (ST) | 122,750 | |
| Embase | S2: Quality of Life (SIT) OR Quality of Life (ST) OR Experience (SIT) OR Personal Experience (SIT) OR Experience (ST) | 1,138,011 | |
| Embase | S3: S1 AND S2 | 6,240 | |
| Embase | S4: Qualitative Research (SIT) OR Qualitative Analysis (SIT) OR Qualitative (ST) OR Interview (SIT) OR Semi-Structured Interview (SIT) OR Interview (ST) | 454,320 | |
| Embase | S5: S3 AND S4 | 288 | 11 |
| Database Total: | | | 11 |
| Cochrane Library | S1: Hepatitis C (ST) | 702 | |
| Cochrane Library | S2: Quality of Life (ST) | 5128 | |
| Cochrane Library | S3: S1 AND S2 | 486 | 0 |
| Database Total: | | | 0 |
| JBICOnNECT+ | S1: Hepatitis C (ST) | 12 | 0 |
| Database Total: | | | 0 |
| PsycINFO | S1: Hepatitis (SIT) OR Toxic Hepatitis (ST) OR Hepatitis C (ST) | 3,032 | |
| PsycINFO | S2: Quality of Life (SIT) OR Quality of Life (ST) OR Life Experiences (SIT) OR Life Changes (SIT) OR Experience (ST) | 534,435 | |
| PsycINFO | S3: S1 AND S2 | 413 | |
| PsycINFO | S4: Qualitative Research (SIT) OR Qualitative (ST) OR Interviews (SIT) OR Interview* (ST) | 358,022 | |
| PsycINFO | S5: S3 AND S4 | 138 | 4 |
| Database Total: | | | 4 |
| ASSIA | S1: Hepatitis C (SIT) OR Hepatitis C (ST) | 1,117 | |
| ASSIA | S2: Quality of Life (SIT) OR Quality of Life (ST) | 14,852 | |
| ASSIA | S3: S1 AND S2 | 44 | 0 |
| Database Total: | | | 0 |

Appendix C

Interview schedules

INTERVIEW 1

1A. Welcome and Introduction

- Thank the participant for agreeing to be interviewed.
- Explain why the participant has been approached for this study and re-state the purpose of the research; to explore patient's views and experiences of having hep C. Go through the participant information sheet allowing time for questions, and review the signed consent form.
- Explain that the interview will be recorded and transcribed, and that quotes from the interview may be used in the final report. Advise that a pseudonym will be assigned to the transcript, and any identifying information will be changed. Ask if the participant wishes to choose their own pseudonym.
- Discuss confidentiality, being explicit that the contents of the interview will not be shared with the clinical team, although they will have access to the final report. Note that the interview transcript may be seen by other members of the small research team however. Advise participant not to disclose illegal activity for which they have not been convicted. Advise that disclosure of sensitive information during the interview (e.g. if 'significant harm' to children is disclosed) would mean the researcher would have a duty to act and confidentiality in that case would be broken.
- Advise that notes may also be taken during the interview.
- Ask whether the participant has any questions and answer appropriately.
- Offer tea/coffee/water if able.

Start the audio recorder

Key Topic Areas for interview 1

- **The experience of diagnosis**
- **The illness experience in everyday life**
- **Treatment knowledge and perception**
- **Future outlook**

Questions in bold are proposed as questions to initiate conversation within each key topic area, with areas for exploration and examples of possible follow up questions given in plain text. Further examples of general prompts and probes are given at the end.

2A. Diagnosis

“I’d like to start by talking about when you were diagnosed. Can you tell me what happened?”

Examples of potential further questions/areas for exploration:

“When were you diagnosed and who told you?”

“What did you know about hep C at the time?”

Explore reaction to diagnosis; if not mentioned prompt:

“How did you react to being told you were hep C positive?”

“What do you think caused you to react in that way?”

“Thinking about the time *before* you were diagnosed with hep C; can you tell me a little about how your life was then?”

Explore drug use and social circumstances/support:

“How do you think you got hep C?”

“Tell me more about who was around at that time; any family? Close friends?”

Probe any mention of stigma or attitudes prior to diagnosis

“How has life been since your diagnosis?”

Explore changes that have occurred:

“Has anything (else) changed?”

“What do you think contributed to/caused [those changes]?”

What is their experience of stigma (explore any mention of both internal and external stigma):

“What was it like telling other people?”; “how did their reaction affect you?”

“How do you feel about having hep C now?”

3A. The Illness Experience in Everyday Life

“I’d like to focus a little more on your day-to-day life now. What’s it like for you having hep C?”

Explore physical, emotional and social impacts of living with hep C:

“Does having hep C affect your life in any way?”

“Has having hepatitis C brought about any changes to your life?”

“What are the downsides to having hep C? Are there any positives?”

“Is there anything you do, or don’t do, because of having hep C?” - “What are the reasons for that?”

“You mentioned _____, can you describe what happens?”

“How do you cope with having hep C?”

Explore the burden of living with hep C and support mechanisms:

“What are the main challenges you face because of having hep C?”

“Is there anyone you can turn to for help?”

“Do things ever get too much...?”

“Is there any other way that hep C affects your daily life that we haven’t talked about yet?”

4A. Treatment Knowledge and Perception

“Can you tell me what you know about the treatment for hep C?”

What level of understanding do participants have about the current treatment options?

“Where do you/would you find out information about hep C treatment?”

“Have you ever had treatment for hep C before?”

“Tell me about that experience, what happened?”

OR

“Do you know anyone who’s been through treatment for hep C? *Have they told you anything about it?*”

“You mentioned new/better drugs, can you tell me more about that? How are they better?”

“How do you feel about hep C treatment?”

What perceptions do participants have about hep C treatment?

“Is treatment something you expect to do? *What are the reasons behind that?*”

“Do you have any concerns or worries about hep C treatment?”

“Has the way you feel about hep C treatment changed at all?”

5A. Future Outlook

“Can you tell me a little about any plans you have for the future?”

“Has having hep C played a part in your plans in any way?”

“Have your plans changed at all?”

“How does looking to the future make you feel? What do you think are the reasons behind that?”

6A. Ending the Interview

“Is there any other way that hep C affects your life that we haven’t discussed, or anything you think it might be important for me to hear that I haven’t asked you about?”

Check information obtained during the interview covers all required patient demographic data.

“Finally, what would you say to someone who had just been diagnosed with hep C today?”

“Has what you would say changed in any way over the years? Why?”

“Would you give any specific advice?”

Stop audio recorder

- Thank the participant for their time and for sharing their experiences. Ask if they have any questions.
- Explain that you are also interested in peoples’ experience of taking hep C treatment, and ask if they would be happy to speak to you again should they begin a course of therapy. If yes, give further details of what this would involve.
- Offer the participant voucher reimbursement for time and expenses

INTERVIEW 2

Revisit the welcome and introduction described in section 1A.

Start the audio recorder

Key Topic Areas for interview 2

- Experience of treatment
- Perceptions of the treatment service
- Suggestions for how the treatment service may be improved

2B. Experience of Treatment

“You’ve just finished your hep C treatment. Can you tell me how that’s been for you?”

Examples of potential further questions/areas for exploration:

Explore any mention of side effects – probe for further detail.

Explore any comparison with previous treatment (will have this information from interview 1).

Explore any mention of coping – support etc., how was this utilised?

Explore any mention of adherence issues.

“What happened? Can you tell me what your treatment period was like?”

“Was there anything you found easier or more difficult than you expected?”

“How did your treatment fit into your daily life?”

“How did taking hep C treatment make you feel?”

“I’ve heard doctors and nurses talking about ‘preparing patients for treatment’. Now you’ve been through treatment, do you think you were prepared for it?”

What is the participant’s view of being prepared for hep C therapy?

Was the emphasis on preparing for treatment from the clinical team appropriate?

Explore any mention of under/over-preparation – in what areas? Why did they feel that way?

“Could you tell me a little about anything you did to prepare for treatment?”

“What advice would you give to someone preparing for treatment now?”

3B. Perceptions of the Treatment Service

“Can you tell me about your relationship with the staff here at RIDU during your treatment?”

Explore the relationship with doctors and specialist nurses

How much contact was there, what was their role?

“Was there anything particularly good or bad that stands out in your mind?” – example.

“How would you rate the treatment service?”

What is the overall perception of being treated for HCV at RIDU?

Explore any positive or negative mentions of HCV drugs specifically (if not already covered)

4B. Suggestions for Improvement

“If you could change anything about the hep C treatment service, what would it be?”

“If you could give advice to someone preparing for treatment now, what would you say?”

5B. Ending the Interview

“Is there anything else that you want to say about the treatment, good or bad, that we haven’t covered already?”

Stop audio recorder

- Thank the participant for their time and for sharing their thoughts and experiences. Ask if they have any questions.
- Explain that you would like to catch up with them again once they know their treatment result, and arrange a date and time if possible (3 months hence).
- Offer the participant voucher reimbursement for time and expenses

Appendix D

Participant Information Sheet



PATIENTS' EXPERIENCES OF HEPATITIS C AND ITS TREATMENT



We would like to invite you to take part in our research study. Before you decide, we would like you to understand why the research is being done and what it would involve for you. Please take time to read the following information and discuss it with others if you wish. One of our team will go through the information sheet with you and answer any questions you might have. We'd suggest this should take around 15 minutes.

Ask us if anything is not clear.

What is the purpose of the study?

The aim of the study is to find out what life is like for people who have hep C. We are interested in what day-to-day life is like, as well as what it's like for people when they take treatment. Knowing how hep C affects people can help doctors and nurses to provide better care for the patients they see.

Why have I been invited to take part?

You have been invited to take part by your doctor/nurse as they know you have hep C.

Do I have to take part?

No. It is entirely up to you whether you decide to join the study. If you agree to take part we will ask you to sign a consent form; however, you are free to withdraw at any time, without giving a reason. A decision not to take part, or to withdraw at any time, will not affect the care you receive.

What will happen to me if I take part?

- If you decide to take part, your doctor/nurse will ask if you agree to your contact details being passed to the study team.
- The study team will then ask you to meet with a researcher for an interview which should last about one hour. The interview will be recorded with a digital audiotape recorder.
- The interview will be held at a time and place convenient for you; this might be where you usually see your doctor/nurse, or maybe in your home. After this, most people's input to the study will be over.
- If you are going to start hep C treatment soon, the researcher may ask if you would be interested in meeting again after your treatment is finished. Agreeing to this part of the study means meeting for another 2 interviews at some point over the next 6 months.

Will I get expenses for taking part?

Yes. At all interviews you will be given a £15 gift voucher to cover any out-of-pocket expenses you might have for taking part.

What are the possible benefits of taking part?

There is no immediate benefit to you, but the information we get from this study could help improve the treatment of people with hep C.

What are the possible risks of taking part?

During the interviews, we ask that you talk as honestly as you can about how living with hep C has been for you. This may be upsetting, and the researcher will ensure your thoughts and feelings are respected.

What will happen if I don't want to carry on with the study?

You may choose to withdraw from the study at any point. If this happens, we will destroy any information already collected from you if that is what you want. At all times, the treatment and care you receive will not be affected.

Will my taking part in this study be kept confidential?

- All information collected about you during the study will be kept strictly confidential. The researcher will ask you to choose a false name, which will then be used to identify you on everything other than the consent form we ask you to sign.
- Your consent form will be kept securely on hospital premises.
- All interviews will be recorded and then written up word-for-word. In addition to using a false name, anything else which could identify you (such as names of friends, family, places near to where to live etc.) will also be changed. Once written up, recordings will be erased from the digital recorder and destroyed completely at the end of the study.
- All written out interviews will be securely disposed of within 5 years. Anonymised quotes may be used in the final report.
- *However, the researcher would need to speak to relevant people if you talk about anything which indicates harm to yourself and others.*

Will my general practitioner (GP) know I have taken part?

Yes, with your consent a letter will be sent to your GP to tell them about your involvement in the study.

What will happen to the results of the study?

The study is part of a post-graduate degree and will be written up as a thesis, as well as being published in academic journals. A summary of results will also be made available in your clinic/surgery.

Who has reviewed and funded this research?

- The work is funded by the Clinical Academic Research Careers (CARC) scheme; a body which includes NHS Lothian, Edinburgh Napier University, Queen Margaret University, the University of Edinburgh and NHS Education Scotland.
- All research in the NHS is looked at by an independent group of people, called a Research Ethic Committee, to protect your interests. This study has been reviewed and given a favourable opinion by South East Scotland Research Ethics Committee 1.

What if there is a problem?

If you have concerns about any aspect of this study, you can speak with an independent person who is not involved with the study; either Sheila Morris, Research Coordinator based at the Western General Hospital. Phone: 0131 537 2842; Email: sheila.morris@luht.scot.nhs.uk; or Norrie Brown, Edinburgh Napier University. Phone: 0131 455 5712; Email: n.brown@napier.ac.uk

If you remain unhappy and wish to complain formally, you can do this by contacting NHS Lothian Customer Relations and Feedback Team, Waverley Gate, 2-4 Waterloo Place, Edinburgh EH1 3EG. Phone: 0131 536 3370; Email: craft@nhslothian.scot.nhs.uk or Barbara Neades, Edinburgh Napier University Ethics Convener, Phone: 0333 900 6040 Email: B.Neades@napier.ac.uk

For further information on this study please contact:

David Whiteley, Substance Misuse Directorate, c/o Ward 41 OPD, Western General Hospital, Crewe Road South, Edinburgh EH4 2XU.

Phone or text: 07972 248470; Email: dwhiteley@nhs.net